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CORRELATES AND PREDICTORS OF APATHY, DEPRESSION AND FATIGUE POST-STROKE

Section A: Correlates and Predictors of Apathy, Depression and Fatigue Post-Stroke: A Systematic Review of the Literature

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CANTERBURY CHRIST CHURCH UNIVERSITY

Doctorate in Clinical Psychology (D.Clin.Psychol.)

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This thesis is the result of my own investigations, except where otherwise stated. Other sources are acknowledged by footnotes giving explicit references. A bibliography is appended.

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Summary of the MRP

A review of the extant literature investigating relationships between apathy, depression and fatigue post-stroke was conducted. This review also looked at common predictors of apathy, depression and fatigue post-stroke. The review indicated that having poorer physical functioning, being female and having a more severe stroke were related to apathy, depression and fatigue. A cross-sectional study, using postal questionnaires was conducted with 63 people aged over 55 years who had a stroke. Participants completed standardised assessments of apathy, depression, fatigue and physical functioning, along with a socio-demographic questionnaire which provided details of demographic information and information about their stroke. In the current study, 60.3% of people were apathetic, 58.7% had depression and 58.7% reported fatigue. Univariate statistics and regression models were used to look at relationships between these constructs and confounding factors. Having poorer physical functioning was the only factor which was associated with apathy, depression and fatigue post-stroke. A Structural Equation Model to account for these relationships was developed and accounted for 58% of the variance in depression scores. Relationships between apathy, depression, fatigue and physical functioning were somewhat different for men and women. Results were discussed in terms of limitations of assessment tools used and clinical implications were proposed.

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Section A: Correlates and Predictors of Apathy, Depression and Fatigue Post-Stroke: A Systematic Review of the Literature

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Abstract

Apathy, depression and fatigue are common sequelae of stroke, and can have an impact on functional recovery. The inter-relations between these common consequences of stroke are poorly understood and the mechanisms of action between them are unclear. A number of associations with apathy, depression and fatigue have been identified, including stroke severity, age and gender. The current review aimed to examine the correlates and predictors of apathy, depression and fatigue in order to better understand how these three constructs interact and to identify any common factors which influence their development post-stroke. A systematic review of the literature was conducted using MEDLINE, PsycInfo, Web of Science and CINAHL. Two hundred and seventy papers were identified of which 82 met inclusion criteria and were included in this review. Results indicated that there was some evidence that apathy and depression were related and strong evidence that depression and fatigue were related; however no studies have examined the relationships between apathy and fatigue post-stroke. Common predictors of all three constructs included poorer physical functioning, female gender and increased severity of stroke. Apathy and fatigue seemed to be linked to biological factors, while depression was linked to biological, psychological and social factors. The correlates and predictors of apathy, depression and fatigue may include factors which can be managed and treated post-stroke.

Stroke is a leading cause of disability in the UK and results in a range of physical, psychological and social consequences (NICE, 2008). While healthcare improves and there is a decrease in mortality rates post-stroke, more people are surviving with health-related difficulties. This is framed within an ageing population where the numbers of people who have a stroke are likely to increase (NICE, 2008).

While increased rates of depression and fatigue have been identified post-stroke, there is little to no evidence available to indicate treatment options to improve depression and fatigue post-stroke (Hackett, Yapa, Parag & Anderson, 2005; McGeough et al., 2009). Apathy, depression and fatigue have been reported to influence functional recovery following a stroke (Delaney & Ravdin, 1997; Glader, Stegmayr & Asplund, 2002; Hama et al., 2007a) and fatigue has been linked with an increase in the likelihood of death post-stroke (Glader et al., 2002).

Apathy has been defined by Marin (1990) as "diminished motivation not attributable to diminished level of consciousness, cognitive impairment, or emotional distress" (p.22). While it has been argued that apathy is a symptom of depression, a more recent study has found that apathy can exist independent of depression (Andersson, Krogstad & Finset, 1999). Brodaty et al. (2005) found that 26.7% of stroke patients had apathy compared to 5.4% in their control group. Age, cognitive functioning and damage to the right hemisphere have been associated with apathy (Andersson et al., 1999; Brodaty et al., 2005).

Rates of post-stroke depression have been reported ranging from 4 – 63% (Hackett et al., 2005). A number of studies have identified predictors of depression including multiple losses, lesion location (Rickards, 2005), time since stroke (Schwartz et al., 1993) female gender, history of depression pre-stroke and living alone (Andersen, Vestergaard, Ingemann-Nielsen & Lauritzen, 1995). Larger volume of brain damage caused by a stroke, disability, severity of the stroke and cognitive impairment have also been associated with depression

(Hackett & Andersen, 2006; Nys et al., 2005). However, there has been some dispute over the relationship between lesion location and post-stroke depression (Carson et al., 2001). There has been debate about whether post-stroke depression occurs as a result of neuroanatomical / organic brain changes or is more reactive in nature and linked to the adjustment to changes associated with a neurological condition. A recent review by Ayerbe, Ayis, Wolfe and Rudd (2013) reported that there was no association between brain lesion location and presence of depression post-stroke. This indicated that post-stroke depression may be influenced by a more reactive or psychological pathway than a neuroanatomical one.

Fatigue is common after stroke, both in the acute stages and at later follow-up (van der Werf et al., 2001). They reported fatigue in 50% of their sample, with only 38% of those with extreme fatigue reporting depression. This indicated that fatigue may exist post-stroke independent of depression. However, Glader et al. (2002) reported that fatigue and depression are associated following stroke. Predictors of post-stroke fatigue have been reported to include female gender, increased age and mental ill-health (Mead et al., 2011; Schepers, Visser-Meily, Ketelaar & Lindeman, 2006).

Bourgeois, Hilty, Chang, Wineinger & Servis (2004) outlined how it can be difficult to distinguish between apathy, depression and fatigue following a stroke. The inter-relations between these common consequences of stroke are poorly understood and the mechanisms of action between them are unclear. It appears that apathy, depression and fatigue are discrete constructs which may overlap for some people post-stroke, and this may be associated with common predictors of the separate constructs, such as age, female gender and lesion location.

Although the large majority of studies which look at treatment for apathy, depression and fatigue relate to pharmacological interventions, there is some evidence that psychological interventions play a role in alleviating some of these symptoms post-stroke (Hackett, Anderson, House & Xia, 2009). It is therefore of value to psychological rehabilitation to be

aware of differences within these constructs in order to best identify and treat apathy, depression and fatigue post-stroke.

Rationale for the Current Study

Having a better understanding of the inter-relationships between the predictors of apathy, depression and fatigue post-stroke, will allow for better assessment, management and treatment of these common psychological sequelae of stroke. A review of the literature may provide a clearer understanding of the inter-connections between apathy, depression and fatigue and their common predictors, which may begin to identify sources for more targeted treatments to support engagement and improve rehabilitation outcomes post-stroke.

Aims of the Current Study

The current study aimed to fill the gap in the literature and provide a systematic review of the published research

1. Looking at inter-relationships between apathy, depression and fatigue post-stroke and
2. To assess if there are identified common factors which may act as predictors of these constructs post-stroke.

Method

Literature Search

A systematic review of the literature was conducted. A broad scoping search of the literature was performed in order to identify key terms that could be used for a more specific search. A range of possible key terms were developed including apathy / motivation, depression / mood / affect, fatigue /tiredness / sleep disorders, stroke / cerebrovascular accident, relationships / predictors / correlations / associations. These were modified within each database to maximise the sensitivity of the search. Exploded Medical Subject Headings (MeSH) were used to ensure that the key words were within the broadest search categories. No time limit on publication was used in order to identify as many papers as possible, and to

track historical information on relationships between apathy, depression and fatigue post-stroke.

Medline, PsycInfo, Web of Science and CINAHL databases were searched with key terms, using advanced search options. Boolean search term 'AND' was used to combine the key words to identify papers which addressed the aims of the review. A combination of Boolean searches was conducted to identify papers which looked at one, two and all three constructs – apathy, depression and fatigue. These allowed for the broadest search results.

Inclusion and Exclusion Criteria

Inclusion criteria were identified as follows:

- Must be an original paper
- Must include participants in the study who have had a stroke
- Must have a standardised valid measure of apathy, depression and / or fatigue
- Must look at apathy, depression and fatigue as outcomes post-stroke
- For Aim 1, must look at the relationship between at least two of the constructs apathy, depression and fatigue post-stroke
- Both cross-sectional and longitudinal studies will be included, but may be treated differently in the analyses

Exclusion criteria:

- Review papers
- Dissertation abstracts / book chapters / not published in peer reviewed journals
- Editorials / letters to editors
- Studies not specific to stroke
- Treatment based studies
- Studies related to Transient Ischaemic Attacks (TIAs)
- Studies where the outcome measures were not related to apathy, depression or fatigue

- Studies not written in / or translated into the English language

Search Strategy

Papers identified within the electronic searches were screened based on their title and brief bibliographic information, they were then screened based on the information in the abstract; articles which did not meet the inclusion criteria were excluded. Full texts of selected papers were retrieved for further analysis.

Data Extraction & Management

A data extraction form (Appendix A) was developed, based on Higgins and Deeks (2008) proposals, in order to extract relevant data, provide a basis to pool data and to assess the quality of the papers.

Results

A broad scoping search of the literature with duplicates removed from within the databases and across databases resulted in 270 papers being identified. These were screened based on title and brief information from the database, and papers which did not match the initial search criteria of not being in English, reviews, letters to editors etc. were excluded. This resulted in 232 papers, which were then screened further in terms of their abstract, which resulted in 99 papers being excluded. Further screening of the full texts of the remaining 133 articles resulted in 82 papers which informed the current review (See Figure 1 for overview). A summary table of these 82 papers is provided in Appendix B.

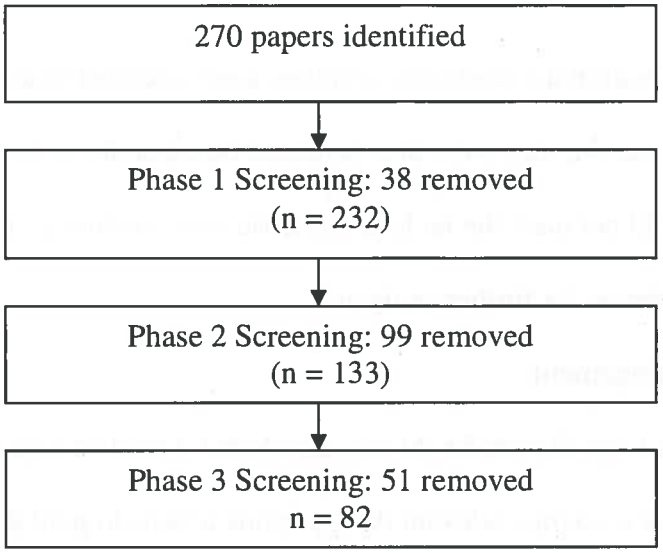

Figure 1 Breakdown of study exclusion at screening phases

Relationships between apathy, depression and fatigue

Papers which focussed on all three constructs, or on two of the three constructs were assessed in order to determine the associations which have been outlined in the literature. This was done in order to determine in what way these constructs interact following stroke. This also allowed an analysis of how apathy, depression and fatigue overlap, or not, following stroke.

Associations between apathy, depression and fatigue. The current review did not identify any original research which looked at these three constructs together.

Associations between apathy and depression. A number of published papers looked at the relationships between apathy and depression following stroke. These included studies looking at differences between groups, correlational studies and regression models to look at how apathy and depression predict the levels of each other following stroke.

Correlational studies. One study identified a significant weak correlation between apathy and self-reported depression (Brodaty et al., 2005). A study by Marin, Firinciogullari

and Biedrzycki (1994) found a significant moderate correlation between self-reported depression (Hamilton scale; Hamilton, 1960) and apathy (AES; Marin, Biedrzycki & Firinciogullari, 1991), but only in left hemisphere stroke survivors, not in right. This correlation was slightly stronger than reported by Brodaty et al. (2005) when both left and right hemisphere survivors were included.

Regression studies. Two studies reported that depression was not a significant predictor of apathy (Caeiro, Ferro & Figueira, 2012; Caeiro, Ferro, Pinho e Melo, Canhão & Figueira, 2013). Caeiro et al.'s (2012) study was made up of people who were in the acute phase post-stroke, less than 4 days since their stroke, while another study (Caeiro et al., 2013) reported the same result in people who were one year post-stroke. Conflicting reports were presented by Yang et al. (2013) and Brodaty, Liu, Withall and Sachdev (2013). Yang et al. (2013) reported that low depression scores were a significant predictor of apathy, within 7 days of stroke, while Brodaty et al. (2013) reported that depression was a significant predictor of apathy at 3-6 months post-stroke; and over time up to 5 years post-stroke. It is difficult to determine any conclusive evidence for a relationship based on these studies, particularly given that conflicting reports are presented within similar time frames since stroke. The two studies looking at the acute phase post-stroke (Caeiro et al., 2012; Yang et al., 2013) used different assessment tools to measure depression. While, the studies looking at longer-term apathy (Brodaty et al., 2013; Caeiro et al., 2013) also used different measures of depression. It is possible that the differences in measurement tools can explain some of the difference in findings.

Differences between groups. Okada, Kobayashi, Yamagata, Takahashi and Yamaguchi (1997) reported that in their sample of stroke survivors, the apathetic group had significantly higher depression score than the non-apathetic group. Onoda et al. (2011) and Tang et al. (2013a) reported similar findings. While, Starkstein, Fedoroff, Price, Leiguarda

and Robinson (1993) reported that in their study, a group of depressed patients were no more likely to have apathy than the non-depressed patients (χ^2= 2.74; df=1; p=NS). However three of these studies used a modified version of the apathy evaluation scale (Okada et al., 1997; Onoda et al., 2011; Starkstein et al., 1993) and each used different measures of depression. Both Starkstein et al.'s (1993) and Onoda et al.'s (2011) studies were conducted in the acute phase post-stroke, while Okada et al. (1997) included both acute and out-patients and assessed people who were on average 16.2 months post-stroke. These factors may account for the differences in results.

Summary. Correlational studies indicated a significant relationship between apathy and depression. Studies using regression models to look at depression as a predictor of apathy found conflicting results, with two reporting depression as a significant predictor of apathy and two reporting a non-significant relationship. Three studies (Okada et al., 1997; Onoda et al., 2011; Tang et al., 2013a) looked at differences between those with and without apathy, and reported that those with apathy had significantly higher depression scores. One study looked at differences between those with depression and those without, and reported that there was no significant difference in apathy scores between these groups. The evidence for a significant relationship between apathy and depression is inconclusive. Indeed, a number of studies reported that there were people who had apathy without the presence of depression, and also that there were people with depression without apathy (Ligthart et al., 2012; Murakami et al., 2013; Withall, Brodaty, Altendorf & Sachdev, 2011).

Associations between apathy and fatigue. The current review did not identify any original research which looked at these two constructs together.

Associations between depression and fatigue. A number of published papers looked at the relationships between depression and fatigue following stroke. These included both correlational studies and regression models to look at how depression and fatigue predict

the levels of each other. They also included studies where differences between groups with the constructs were examined.

Correlational studies. Two studies reported that depression and fatigue are significantly moderately correlated (Hubacher et al., 2012; Park et al., 2009). Both studies used the Beck Depression Inventory (BDI; Beck, Steer & Brown, 1996) and the Fatigue Severity Scale (FSS; Krupp, LaRocca, Muir-Nash & Steinberg, 1989) to assess depression and fatigue respectively. Participants in both studies were of similar age and time since stroke.

Regression studies.

Depression as outcome in regression. In four studies where depression was the outcome measure in regression models, fatigue was found to be a significant predictor of depression in three studies, while in one study (Schepers et al., 2009) it was not a significant predictor of depression score / presence of depression. All studies used the same measure of fatigue (FSS), while three different measures of depression were used. Interestingly two studies which used the same measure (Center for Epidemiologic Studies Depression Scale (CES-D; Eaton, Muntaner, Smith, Tien & Ybarra, 2004) found contradictory results (Schepers et al., 2006; van de Port, Kwakkel, Bruin & Lindeman 2007). Both of these studies were well powered, included similar age groups and assessed people at similar period after stroke – three years, thus the contradictory findings cannot be explained by these factors.

Fatigue as outcome in regression. In twelve studies where fatigue was looked at as the outcome measure in regression models, depression was found to be a significant predictor of fatigue in all studies. Studies used a number of different measures to assess fatigue and depression, and different regression models were used including both linear and logistical models. One study by Appelros (2006) used DSM-IV (American Psychiatric Association,

2000) criteria to assess for presence of clinical depression. All bar two studies (Tseng, Billinger, Gajewski, & Kluding, 2010; Vuletic, Lezaic & Morovic, 2011) were well powered and had sufficient numbers to ensure valid models. Studies included participants who had their stroke from the acute phase to 4.1 years post-stroke and had mean ages of 50, 60 and 69 years, thus these results appear to occur irrespective of age and time since stroke.

Differences between groups. Four studies looked at the differences between those stroke survivors who were fatigued and those who were not. Two studies found depression scores were significantly increased for those who were fatigued, compared to those who were not fatigued. Two studies reported no significant difference between those who were fatigued and those who were not on depression scores. The same measure of fatigue (FSS) was used in all studies, while different measures of depression were used across the studies. Studies reporting a significant difference in depression scores between fatigued and non-fatigued groups assessed people at three months post-stroke, while one of the studies not finding a significant relationship (Park et al., 2009) assessed people at a later stage, on average at 32.7 months post-stroke.

Summary. Depression and fatigue appeared to be significantly correlated post-stroke (Hubacher et al., 2012; Park et al., 2009). In regression models where depression was the outcome, fatigue was a significant predictor in four out of five studies. In regression models where fatigue was the outcome, all studies reported that depression was a significant predictor of fatigue. There was no conclusive evidence for a difference in depression scores between groups of people with and without fatigue. Looking at the evidence examining the relationship between depression and fatigue in stroke survivors indicated that there was a significant relationship between depression and fatigue in this group.

Overall summary. The current review did not identify any original research which looked at apathy, depression and fatigue together, nor did it identify any original research

looking at apathy and fatigue. Although there have been many reports in the general literature about the overlap of apathy and depression, the evidence for a significant relationship between apathy and depression in stroke survivors was inconclusive. There did appear to be a body of evidence to indicate that there was a significant relationship between depression and fatigue in stroke survivors.

Studies are difficult to compare given different measures used to assess apathy, depression and fatigue, different age profiles of respondents, acute versus later stages of stroke, and type of stroke included or excluded from the study.

Common factors related to apathy, depression and fatigue

Papers which identified factors which predicted depression, apathy and / or fatigue post-stroke were identified and will be outlined below. This provided information on factors which may predict one, two or all three of these constructs. A large number of papers (n=22) reported findings related to cognitive functioning and apathy, depression and / or fatigue; these were excluded from the analyses as it was deemed that covering this broad area was beyond the scope of this review. These studies used a number of measures of cognition ranging from cognitive screening tools such as the MMSE, to measures of more specific cognitive functioning such as executive functioning. As such, it would have been difficult to synthesis the findings within the limitations of the current review.

Neuroanatomical factors.

Lesion location. Eight studies investigated the associations between apathy and lesion location, with three reporting non-significant associations (Caeiro et al., 2013; Castellanos-Pinedo et al., 2011; Okada et al., 1997) and five reporting significant associations. Of the five studies reporting significant associations, only two reported similar brain regions. Tang et al. (2013a) reported that those with post-stroke apathy were more likely to have acute pontine infarcts (brainstem region) and Murakami et al. (2013) reported

that in those with apathy, there was lesion overlap on the brainstem and bilateral striatum. Starkstein et al. (1993) also reported that apathy was associated with lesions in the posterior limb of the internal capsule. Conflicting findings were provided by Quaranta, Marra and Gainotti (2012) and Yang et al. (2013). Quaranta et al. (2012) reported associations with the anterior brain, and found that left anterior lesions predicted reduced motivation; similarly, Yang et al. (2013) reported a significant difference between those with and without apathy on frontal lesion location.

Twenty studies looked at the associations between depression and lesion location. Of these, fourteen reported no association between post-stroke depression and lesion location (Aben et al., 2006; Altieri et al., 2012; Berg, Palomaki, Lehtihalmes, Lonnqvist, & Kaste, 2003; Caeiro, Ferro, Santos & Figueira, 2006; Carota et al., 2005; Chau et al., 2010; Dam, 2001; Kaji, Hirata & Ebata, 2006; Kouwenhoven, Gay, Bakken and Lerdal, 2013; Nys et al., 2005; Rush et al., 2010; Weaver, Page, Sheffler & Chae, 2013; Yang et al., 2013; Zhang, Pan, Wang & Zhao, 2013). However, four studies reported significant relationships between infarcts in the frontal lobe and higher rates of depression (Effat, Mohamed, El Essawy, El Sheikh & Abdul Aal, 2011; Hama et al., 2007b; Tang et al., 2011; Zhang et al., 2012). These four studies were conducted in three different countries, Egypt, Japan and two in China. The studies used different measures to assess depression including the Hamilton rating scale for depression, Zung self-rating depression scale and DSM-IV criteria for depression. The results indicating that depression is associated with lesions in the frontal region are therefore cross-cultural and not dependent on the measurement tool used. None of the studies specified specific regions in the frontal region. Hama et al. (2007b) reported that depression was associated with left frontal lesions, while the other studies did not report lateralisation. Two studies reported significant associations between lateralisation and depression, however these were contradictory. MacHale, O'Rourke, Wardlaw & Dennis (1998) reported that depression

was significantly associated with right cerebral hemisphere compared to left hemisphere, while Paradiso and Robinson (1999) reported that minor depression was associated with left-hemisphere lesion location. One study by Murakami et al. (2013) reported that for those with depression there were more likely to be lesions in the brainstem.

Six studies looked at the associations between fatigue and lesion location with four (Choi-Kwon, Han, Kwon & Kim, 2005; Hsieh & Kao, 2005; Ingles, Eskes & Phillips, 1999; Radman et al., 2012) reporting no significant associations. A study by Snaphaan, van der Werf and de Leeuw (2011) reported that the presence of an infratentorial infarct was a significant risk factor for fatigue, compared to other locations. Kutlubaev et al. (2013) reported no association between post-stroke fatigue and side of lesion, but reported that fatigue scores were higher in patients with posterior strokes. These two studies may indicate some role for posterior regions in the development of post-stroke fatigue, though further work would be required in order to provide evidence of a role. Overall, there was no strong evidence for a role of lesion location in post-stroke fatigue.

Summary. Evidence from the literature does not suggest any strong association between the development of post-stroke apathy, depression or fatigue, and lesion location. While a small number of studies (four) have identified some links between depression and infarcts in the frontal region, and two studies reported links between fatigue and posterior areas, this requires further investigation.

Basal Ganglia. There appeared to be some evidence to suggest a role for the basal ganglia in the development of post-stroke apathy and depression though evidence was limited. There were conflicting results in relation to the association between the basal ganglia and fatigue.

Hama et al. (2007b) reported that apathy was related to damage to the bilateral basal ganglia, while Onoda et al. (2011) reported that apathy was associated with lesions in the left basal ganglia.

Chatterjee, Fall & Barer (2010) reported that those people with post-stroke depression had more changes in basal ganglia compared to those without depression. Murakami et al. (2013) reported similar findings that for those with depression there were more likely to be lesions in the left basal ganglia.

Tang et al. (2013b) reported that strokes in structures within the basal ganglia were more common in those people who had post-stroke fatigue, compared to those without fatigue. However, Naess, Lunde, Brogger and Waje-Andreassen (2012a) reported no association between basal ganglia stroke and fatigue.

Cerebral blood flow. Only one identified study looked at the role of cerebral blood flow and its relationship to apathy. Okada et al. (1997) reported that regional cerebral blood flow (rCBF) of the bilateral hemisphere was significantly lower in the apathetic group than in the non-apathetic group. They further reported that the apathetic group showed significantly reduced rCBF in the right dorsolateral frontal and left frontotemporal regions, and that rCBF in the basal ganglia was reduced for the apathetic group compared with the non-apathetic group.

Overall summary of neuroanatomical factors. The findings from this review indicated that there is inconclusive evidence for any neuroanatomical roles in the development of post-stroke apathy, depression and fatigue. There was some evidence for an association between frontal lobe lesions and post-stroke depression; and for an association between lesions in the basal ganglia and apathy and depression.

Physical functioning. Looking at the literature focusing on the relationship between physical functioning and apathy, depression and fatigue identified some interesting findings.

There appeared to be slightly more evidence for a significant relationship between physical functioning and apathy, than no association. Five studies reported a significant relationship, with all five finding a relationship between higher rates of apathy and more difficulties with physical functioning (Brodaty et al., 2005; Brodaty et al., 2013; Caeiro et al., 2013; Mikami, Jorge, Moser, Jang & Robinson, 2013; Tang et al., 2013a). Three papers reported a non-significant relationship.

There were conflicting reports regarding the relationship between depression and physical functioning post-stroke, however there was strong evidence that poorer physical functional was associated with higher levels of depression. Of 29 papers which reported on the association, 21 reported a significant relationship between depression and physical functioning, with five reporting a non-significant relationship. Twenty out of 21 studies reporting significant relationships found that lower physical functioning was associated with more depression (Ayerbe, Ayis, Rudd, Heuschmann & Wolfe, 2011; Badaru, Ogwumike, Adeniyi & Olowe, 2013; Brown, Hasson, Thyselius & Almborg, 2012; Carota et al., 2005, Chau et al., 2010; Effat et al., 2011, Hackett & Andersen, 2006; Haghgoo, Pazuki, Hosseini & Rassafiani, 2013; Hilari et al., 2010– at 3 & 6 months post-stroke; Hsieh & Kao, 2005; Ku et al., 2013; Lam, Lee & To, 2010; MacHale et al., 1998; Naess, Lunde & Brogger, 2012b; Nys et al., 2005; Quaranta et al., 2012; Raju, Sarma & Pandian, 2010; Sienkiewicz-Jarosz et al., 2010; Townend, Tinson, Kwan & Sharpe, 2010; Zhang et al., 2013). One study by Berg et al. (2003) reported that higher levels of physical functioning in the acute phase post-stroke was significantly associated with higher levels of depression.

Similar to the relationship with depression, there were conflicting reports of the relationship between fatigue and physical functioning; however, the literature does not identify any specific trend in the findings. Fourteen studies reported on the association between fatigue and physical functioning. Of these, seven reported non-significant

relationships, while seven reported significant associations. All of the studies reporting a significant association between physical functioning and fatigue found that lower physical functioning was associated with greater levels of fatigue (Appelros, 2006; Choi-Kwon et al., 2005; Christensen et al., 2008; Feigin et al., 2012; Lerdal et al., 2011; Naess et al., 2012b; Naess, Nyland, Thomassen, Aarseth, & Myhr 2005; Tang et al., 2013b).

Overall, there was some evidence for an association between poorer physical functioning and apathy, and strong evidence for an association between poorer physical functioning and depression. The evidence related to associations between physical functioning and fatigue was mixed, however in studies which did report a significant relationship they all found that poorer physical functioning was significantly related to increased levels of fatigue.

Gender. Of three studies looking at the association of gender and apathy, only one reported a significant association. Kaji et al. (2006) reported that female gender was a significant predictor of apathy in a regression model.

Twenty studies looked at the relationship between gender and depression. Studies by Berg et al. (2003) and Brown et al. (2012) reported conflicting results across time points. Berg et al. (2003) reported that male sex was significantly associated with higher rates of depression at 18 months post-stroke, but not at the acute phase, 2, 6 or 12 months post-stroke. Brown et al. (2012) reported that females were significantly more depressed than males at two weeks post discharge, but not at three months or 12 months post discharge. These results are contradictory and do not provide a clear picture of the interaction between gender, depression and time since stroke. Eighteen other studies looked at the relationship between gender and post-stroke depression. Of these, seven reported non-significant associations, while 11 reported significant associations. Nine studies (Angelelli et al. , 2004; Dam, 2001; Haghgoo et al., 2013; Hsieh & Kao, 2005; Quaranta et al., 2012; Tang et al., 2011; Townend

et al., 2010; Weaver et al., 2013; Zhang et al., 2013) reported that females were significantly more likely than males to develop higher rates of post-stroke depression. Two studies reported that males were more likely to be depressed than females (Effat et al., 2011, Schepers et al., 2009).

Eight studies investigated the relationship between gender and post-stroke fatigue, with four reporting significant relationships and four reporting non-significant associations. The four studies reporting significant associations between gender and fatigue found that female gender was associated with higher levels of fatigue, compared to male (Crosby, Munshi, Karat, Worthington & Lincoln, 2012; Kutlubaev et al., 2013; Mead et al., 2011; Tang et al., 2013b).

Overall it appeared that female gender was more likely than male to be associated with apathy, depression and fatigue post-stroke.

History of mental health difficulties. There were no identified studies looking at the relationship between previous mental health and apathy. Only one study looked at this as a variable for fatigue and reported a significant relationship between pre-stroke depression and post-stroke fatigue (Naess et al., 2012b). Five studies looked at the relationship between previous mental health and post-stroke depression, with four of these reporting a significant relationship between pre-stroke depression and post-stroke depression (Hackett & Andersen, 2006; Quaranta et al., 2012; Tang et al., 2011; Taylor-Piliae, Hepworth & Coull, 2013).

Social support. Within the current review, four studies were identified which outlined the relationship between social support and post-stroke depression. No studies were identified referring to social support and apathy or fatigue. All four studies reported a significant relationship between depression and social support, with lower levels of social support significantly associated with higher rates of depression (King, Shade-Zeldow,

Carlson, Feldman & Philip, 2002; Lam et al., 2010; Li, Wang & Lin, 2003; Taylor-Piliae et al., 2013).

Age. It appeared that age was significantly associated with apathy post-stroke, with six out of seven studies reporting a significant relationship. Older age was associated with higher rates of apathy (Brodaty et al., 2005; Quaranta et al., 2012; Santa et al., 2008; Starkstein et al., 1993; Tang et al., 2013b; Yang et al., 2013).

There was inconclusive evidence for a relationship between age and depression post-stroke, and the direction of this relationship. Studies by Greenop, Almeida, Hankey, van Bockxmeer and Lautenschlager (2009) and Hilari et al. (2010) reported contradictory findings within their studies. Greenop et al. (2009) found a non-significant correlation between depression as measured on the Neuropsychiatric Inventory – depression subscale (NPI; Cummings et al., 1994) and age, but a significant relationship between depression and age using the Hospital Anxiety and Depression Scale – depression subscale (HADS-D; Zigmond & Snaith, 1983). Hilari et al. (2010) reported a significant relationship between psychological distress as measured by the General Health Questionnaire-12 (GHQ-12; Goldberg, 1972) and younger age at baseline assessment, but not at 3 and 6-months post-stroke. This indicated that the time since stroke may be an interacting factor in the relationship between age and depression. Also measurement tools may not be sensitive to differences in mood for different age groups. Seventeen other studies presented findings related to age and depression, with seven reporting significant associations and ten reporting no significant associations. Two studies reported that older age was significantly associated with higher rates of depression (Berg et al., 2003; Lincoln et al., 2013). Five studies found that younger age was significantly associated with higher rates of depression (Carota et al., 2005; Effat et al., 2011, Fuller-Thompson, Tulipano & Song, 2012; MacHale et al., 1998;

Paradiso & Robinson, 1999). While the relationship between age and depression was not conclusive, it seemed likely that younger age is associated with post-stroke depression.

Similar to depression, it was not clear from the literature whether or not age was related to post-stroke fatigue, nor the direction of this relationship. Nine studies reported on the relationship, with six reporting non-significant associations and three reporting significant relationships between age and post-stroke fatigue. Two studies found that increasing age was associated with higher levels of fatigue (Feigin et al., 2012; Mead et al., 2011), while a study by Snaphaan et al. (2011) found that younger age was related to post-stroke fatigue.

Time since stroke. Two studies looked at the relationship between apathy and time since stroke and reported a significant relationship, with increased time since stroke linked to increased rates of apathy (Angelelli et al., 2004; Brodaty et al., 2013). Angelelli et al. (2004) reported that there was a greater risk of developing apathy at six months and one year post-stroke than in the post-acute phase. Brodaty et al. (2013) reported that the risk of developing stroke increased as time since stroke increased, with more apathy reported at 3-6 months, 1 year, 3 years and 5 years post-stroke.

Five studies investigated the association between time since stroke and depression, with two reporting non-significant relationships and three reporting significant relationships. Two studies reported that levels of depression increase over time (Gainotti, Azzoni & Marra, 1999; Thompson, SobolewShubin, Graham & Janigian, 1989), while a study by King et al. (2002) reported that there was a significant decrease in depression scores from the acute phase to 2 years post discharge. It is difficult to compare these findings as the time since stroke varies across studies and how it is measured also varied. Thompson et al. (1989) used a continuous variable of time since stroke to examine the effect of time looking at people an average of nine months post-stroke (range: 1-60 months). Gainotti et al. (1999) and King et al. (2002) both measured people at different time points. Gainotti et al.'s (1999) study refers

to differences measured at less than two months since stroke, between 2 - 4 months and over four months since stroke, which represents a shorter time frame than both other studies. As such, it is difficult to interpret these amalgamated results.

Six studies looked at the relationship between time since stroke and fatigue, with all six reporting no significant association. One study by Christensen et al. (2008) reported significant declines in levels of fatigue between 10 days and 3 months after stroke, but found that they did not change from then until 1 and 2 years post-stroke.

The evidence for associations between time since stroke and apathy and depression is inconclusive. There were conflicting accounts of the relationship between depression and time since stroke, with one study reporting a decrease in depression over time and others reporting an increase. These studies are difficult to compare due to differences in the time periods being examined. There appeared to be strong evidence to suggest that there was not an association between fatigue and time since stroke.

Type of stroke. One study looked at the association between apathy and type of stroke. Caeiro et al. (2012) reported a significant relationship and found that cerebral haemorrhage was a significant predictor of apathy, compared to other stroke types.

Six studies investigated the relationships between depression and type of stroke with none reporting a significant relationship.

Two studies looked at the associations between fatigue and type of stroke and both reported no significant association (Appelros, 2006; Crosby et al., 2012).

There is no clear evidence to suggest a relationship between type of stroke and post-stroke apathy, depression or fatigue.

Severity of stroke. Three studies looked at the relationship between stroke severity and the development of post-stroke apathy. Two studies reported no significant associations (Brodaty et al., 2005; Yang et al., 2013). A study by Tang et al. (2013a) reported that

patients with apathy had significantly higher levels of stroke severity than those without apathy.

Eight studies looked at the relationship between depression and stroke severity, with six of these reporting significant relationships between depression and stroke severity. The majority of these studies (n = 4) used the National Institutes of Health Stroke Scale (NIHSS) to assess stroke severity. While two studies used the Glasgow coma scale and the Scandinavian stroke scale. All of the studies reporting a significant relationship found that increased stroke severity was associated with higher levels of depression (Ayerbe et al., 2011; Berg et al., 2003; Hilari et al., 2010; Raju et al., 2010; Sienkiewicz-Jarosz et al., 2010; Tang et al., 2011).

Five studies reported on the associations between fatigue and stroke severity with conflicting findings. Three studies (Ingles et al., 1999; Kutlubaev et al., 2013; Tang et al., 2013b) reported no significant relationship between fatigue and stroke severity, while two reported significant associations. Appelros (2006) and Winward, Sackley, Metha & Rothwell (2009) both reported that more severe stroke was associated with higher levels of fatigue.

Overall, it appeared that stroke severity was associated with higher levels of depression after stroke, while the relationship between fatigue and stroke severity was less clear.

Discussion

Despite a wealth of research being conducted in relation to the psychological sequelae of stroke, there are many conflicting reports in the literature. The current review had two aims, firstly to look at the relationships identified within the literature in relation to apathy, depression and fatigue within stroke populations; and secondly to identify any common predictors of these constructs within these populations.

Relationships between apathy, depression and fatigue

There were no studies identified which looked at the relationships between apathy, depression and fatigue; and no studies looked at the links between apathy and fatigue. The evidence from the literature for a relationship between apathy and depression was inconclusive. This was a somewhat surprising result given that it has been reported that apathy is a symptom of depression. Based on the literature reviewed, it seemed that these are separate constructs which often overlap, but can occur independently post-stroke. Studies which looked at the relationship between apathy and depression used different measurement tools for depression and it is likely that different items on these scales pick up or dismiss elements of apathy. Both studies (Caeiro et al., 2012; Caeiro et al., 2013) reporting non-significant results on regression models used the Montgomery-Asberg Depression Scale (Montgomery & Asberg, 1979) where one of the 10 items refers to 'Inability to feel' which asks about motivation and interest. It is surprising therefore that given that this scale is heavily weighted by elements of apathy, that the results were insignificant.

There was a large body of evidence to indicate that there was a significant relationship between depression and fatigue in stroke survivors, with 12 studies reporting regression models where depression was a significant predictor of fatigue, and four studies where fatigue was a significant predictor of depression. These findings were reported in studies which included people at different stages post-stroke, from acute phase up to three years post-stroke, and with different measurement tools for depression used. No longitudinal studies looking at the time line of the development of post-stroke depression and / or fatigue have been completed and as such it is not possible to determine whether fatigue leads to depression or vice versa, or whether they occur simultaneously.

Common predictors of apathy, depression and fatigue

Looking at the common predictors identified within studies and their relationship to post-stroke apathy, depression and fatigue identified some interesting findings. In terms of apathy, there was evidence for a link with the basal ganglia, poorer physical functioning and older age. In terms of depression, there was strong evidence for significant relationships with poorer physical functioning, female gender, pre-stroke depression, lack of social support and stroke severity. Along with this, there was some evidence for relationships between frontal lesions, basal ganglia and younger age. In terms of fatigue, there was evidence for significant relationships with poorer physical functioning and female gender. There was some evidence for a role of the posterior brain regions in the development of post-stroke fatigue. Common predictors of apathy, depression and fatigue therefore included poorer physical functioning and female gender.

There was a wide body of literature published looking at the correlates and predictors of post-stroke depression; with less publications looking at apathy and fatigue. Generally studies were of a high quality, with the majority published in high impact journals. A number of studies where regression models were completed were underpowered and results from these studies should be interpreted with caution (Taylor-Piliae et al., 2013; Tseng et al., 2010; Vuletic et al., 2011). Studies were conducted across 24 different countries, with the majority carried out in Europe, the USA and Australia. Some of the findings may be influenced by cultural differences, which may be linked to the management and treatment of people who have had a stroke with different healthcare settings and different cultural norms.

A number of methodological limitations were identified in the studies conducted. Some studies did not differentiate between the time since stroke nor did they take account of differences between people's levels of apathy, depression and fatigue between the acute stages post-stroke and longer-term studies. This difference in time since stroke has

implications in terms of people's adjustment and realisation of the disabilities and loss associated with stroke and the implications that it may have on daily functioning once they have returned to their communities. This review identified that studies which did account for time since stroke showed that levels of apathy and depression increased over time. However, this was not the case for fatigue.

Similarly, studies which looked at age at stroke onset and apathy, depression and fatigue indicated that increased age was related to apathy; however not all studies took age into consideration and included people from diverse age ranges including working age to older aged individuals. The sense of loss of role in not being able to return to work, may have a greater impact on post-stroke depression than for older people who do not experience that loss of role and there was some indication that this was the case from this review.

As was mentioned earlier, different measurement tools resulted in conflicting findings in the studies reviewed. The majority of studies used the apathy evaluation scale (AES; Marin et al., 1991) and the fatigue severity scale (FSS; Krupp et al., 1989) to measure apathy and fatigue. A range of different tools were used to assess for depression including the DSM-IV criteria, Montgomery-Asberg Depression Scale, Geriatric Depression Scale, Hamilton Depression Scale, Beck Depression Inventory-II, Center for Epidemiologic Studies Depression Scale, Hospital Anxiety and Depression Scale. With the exception of the Geriatric Depression Scale, these tools are normed for a broad range of ages, and do not specifically aim to assess for depression in older age. Given that the majority of people who have a stroke are older, it seems that these tools do not take account of specific manifestations of depression in older age. These depression tools include a variety of items and some include an overlap with apathetic and fatigue symptoms, and as such may find it more difficult to differentiate between these constructs. These factors may have impacted on the results of the studies reviewed.

This literature review indicated that apathy and fatigue were more influenced by biological factors, such as lesion location, poorer physical functioning, gender and age; whereas depression was related to biological, psychological and social factors. The current study identified a gap in the literature in terms of an understanding of how apathy, depression and fatigue inter-relate post-stroke. While there have been many studies which look at the predictors of apathy, depression and fatigue, to date no study has looked at common predictors in a way which could provide a better understanding of the manifestation of inter-relations in these post-stroke sequelae. This may provide some guidance for a more effective way to assess, manage and treat people with post-stroke apathy, depression and fatigue.

References

*References marked with an asterix were included in the literature review.

*Aben, I., Ladder, J., Honig, A., Lousberg, R., Boreas, A., & Verhey, F.R.J. (2006). Focal or generalized vascular brain damage and vulnerability to depression after stroke: A 1-year prospective follow-up study. *International Psychogeriatrics, 18*(1), 19-35. doi:10.1017/S104161020500270X

*Altieri, M., Maestrini, I., Mercurio, A., Troisi, P., Sgarlata, E., Rea, V., . . . Lenzi, G. L. (2012). Depression after minor stroke: Prevalence and predictors. *European Journal of Neurology, 19*(3), 517-521. doi:10.1111/j.1468-1331.2011.03583.x

American Psychiatric Association. (2000). *Diagnostic and statistical manual of mental disorders* (4th Ed.). Washington, DC: APA.

Andersen, G., Vestergaard, K., Ingemann-Nielsen, M., & Lauritzen, L. (1995). Risk factors for post-stroke depression. *Acta Psychiatrica Scandinavica, 92*(3), 193-198. doi:10.1111/j.1600-0447.1995.tb09567.x

Andersson, S., Krogstad, J.M., & Finset, A. (1999). Apathy and depressed mood in acquired brain damage: Relationship to lesion localization and psychophysiological reactivity. *Psychological Medicine, 29*(2), 447-456. doi:10.1017/S0033291798008046

*Angelelli, P., Paolucci, S., Bivona, U., Piccardi, L., Ciurli, P., Cantagallo, A., . . . Pizzamiglio, L. (2004). Development of neuropsychiatric symptoms in poststroke patients: A cross-sectional study. *Acta Psychiatrica Scandinavica, 110*(1), 55-63. doi: 10.1111/j.1600-0447.2004.00297.x

*Appelros, P. (2006). Prevalence and predictors of pain and fatigue after stroke: A population-based study. *International Journal of Rehabilitation Research, 29*(4), 329-333. doi:10.1097/MRR.0b013e328010c7b8

*Ayerbe, L., Ayis, S., Rudd, A. G., Heuschmann, P. U., & Wolfe, C. D. (2011). Natural history, predictors, and associations of depression 5 years after stroke: The South London stroke register. *Stroke, 42*(7), 1907-1911. doi:10.1161/STROKEAHA.110.605808

Ayerbe, L., Ayis, S., Wolfe, C.D.A., & Rudd, A.G. (2013). Natural history, predictors and outcomes of depression after stroke: Systematic review and meta-analysis. *British Journal of Psychiatry, 202,* 14–21. doi:10.1192/bjp.bp.111.107664

*Badaru, U.M., Ogwumike, O.O., Adeniyi, A.F., & Olowe, O.O. (2013). Variation in functional independence among stroke survivors having fatigue and depression. *Neurology Research International, 842980.* Published online Sep 11, 2013. doi:10.1155/2013/842980

Beck, A. T., Steer, R. A., & Brown, G. K. (1996). *Manual for the Beck Depression Inventory-II.* San Antonio, TX: Psychological Corporation.

*Berg, A., Palomaki, H., Lehtihalmes, M., Lonnqvist, J., & Kaste, M. (2003). Poststroke depression: An 18-month follow-up. *Stroke, 34*(1), 138-143. doi:10.1161/01.STR.0000048149.84268.07

Bourgeois, J.A., Hilty, D.M., Chang, C.H., Wineinger, M.A., & Servis, M.E. (2004). Poststroke neuropsychiatric illness: An integrated approach to diagnosis and management. *Current Treatment Options in Neurology, 6*(5), 403-420. doi:10.1007/s11940-996-0031-9

*Brodaty, H., Liu, Z., Withall, A., & Sachdev, P. S. (2013). The longitudinal course of post-stroke apathy over five years. *The Journal of Neuropsychiatry and Clinical Neurosciences, 25*(4), 283–291. doi:10.1176/appi.neuropsych.12040080

*Brodaty, H., Sachdev, P. S., Withall, A., Altendorf, A., Valenzueela, M. J., & Lorentz, L. (2005). Frequency and clinical, neuropsychological and neuroimaging correlates of

apathy following stroke – the Sydney Stroke Study. *Psychological Medicine, 35,* 1–10. doi:10.1017/S0033291705006173

*Brown, C., Hasson, H., Thyselius, V., & Almborg, A.H. (2012). Post-stroke depression and functional independence: A conundrum. *Acta Neurologica Scandinavica, 126*(1), 45-51. doi:10.1111/j.1600-0404.2011.01595.x

*Caeiro, L., Ferro, J.M., & Figueira, M.L. (2012). Apathy in acute stroke patients. *European Journal of Neurology, 19*(2), 291-297. doi:10.1111/j.1468-1331.2011.03508.x

*Caeiro, L., Ferro, J. M., Pinho e Melo, T., Canhão P., & Figueira, M.L. (2013). Post-Stroke Apathy: An Exploratory Longitudinal Study. *Cerebrovascular Diseases, 35*(6), 507-513. doi:10.1159/000350202

*Caeiro, L., Ferro, J.M., Santos, C.O., & Figueira, M.L. (2006). Depression in acute stroke. *Journal of Psychiatry & Neuroscience, 31*(6), 377-383. Retrieved from: www.ncbi.nlm.nih.gov/pmc/articles/PMC1635801/pdf/20061100s00003p377.pdf

*Carota, A., Berney, A., Aybek, S., Laria, G., Staub, F., GhikaSchmid, F., . . . Bogousslavsky, J. (2005). A prospective study of predictors of poststroke depression. *Neurology, 64*(3), 428-433. doi:10.1212/01.WNL.0000150935.05940.2D

Carson, A.J., MacHale, S., Allen, K., Lawrie, S.M., Dennis, M., House, A., & Sharpe, M. (2001). Depression after stroke and lesion location: A systematic review. *Lancet, 356,* 122-126. doi:10.1016/S0140-6736(00)02448-X

*Castellanos-Pinedo, F., Maria Hernandez-Perez, J., Zurdo, M., Rodriguez-Funez, B., Maria Hernandez-Bayo, J., Garcia-Fernandez, C., . . . Antonio Castro-Posada, J. (2011). Influence of premorbid psychopathology and lesion location on affective and behavioral disorders after ischemic stroke. *Journal of Neuropsychiatry and Clinical Neurosciences, 23*(3), 340-347. doi:10.1176/appi.neuropsych.23.3.340

*Chatterjee, K., Fall, S., & Barer, D. (2010). Mood after stroke: A case control study of biochemical, neuro-imaging and socio-economic risk factors for major depression in stroke survivors. *BMC Neurology, 10,* 125-135. doi:10.1186/1471-2377-10-125

*Chau, J.P.C., Thompson, D.R., Chang, A.M., Woo, J., Twinn, S., Cheung, S.K., & Kwok, T. (2010). Depression among Chinese stroke survivors six months after discharge from a rehabilitation hospital. *Journal of Clinical Nursing, 19*(21-22), 3042-3050. doi:10.1111/j.1365-2702.2010.03317.x

*Choi-Kwon, S., Han, S.W., Kwon, S.U., & Kim, J.S. (2005). Poststroke fatigue: Characteristics and related factors. *Cerebrovascular Diseases, 19*(2), 84-90. doi:10.1159/000082784

*Christensen, D., Johnsen, S.P., Watt, T., Harder, I., Kirkevold, M., & Andersen, G. (2008). Dimensions of post-stroke fatigue: A two-year follow-up study. *Cerebrovascular Diseases, 26*(2), 134-141. doi:10.1159/000139660

*Crosby, G.A., Munshi, S., Karat, A.S., Worthington, E., & Lincoln, N.B. (2012). Fatigue after stroke: Frequency and effect on daily life. *Disability & Rehabilitation, 34*(8), 633-637. doi:10.3109/09638288.2011.613517

Cummings, J., Mega, M., Gray, K., Rosenberg-Thompson, S., Carusi, D. A., & Gornbein, J. (1994). The Neuropsychiatric Inventory: Comprehensive assessment of psychopathology in dementia. *Neurology, 44*, 2308-2314.

*Dam, H. (2001). Depression in stroke patients 7 years following stroke. *Acta Psychiatrica Scandinavica, 103,* 287-293. doi:10.1034/j.1600-0447.2001.103004287.x

Delaney, R.C., & Ravdin, L.D. (1997). The neuropsychology of stroke. In P.D. Nussbaum (Ed.), *Handbook of neuropsychology and aging (pp.315-318).* New York: Plenum Press.

Eaton, W.W., Muntaner, C., Smith, C., Tien, A., & Ybarra, M. (2004). Center for Epidemiologic Studies Depression Scale: Review and revision (CESD and CESD-R). In: M.E. Maruish (Ed.), *The Use of Psychological Testing for Treatment Planning and Outcomes Assessment*. (363-377). Mahwah, NJ: Lawrence Erlbaum.

*Effat, S.M., Mohamed, M.M., El Essawy, H.I., El Sheikh, M.M., & Abdul Aal, H.S. (2011). Predictors and consequences of post-stroke depression in a sample of Egyptian patients. A*rab Journal of Psychiatry, 22*(1), 19-26. Retrieved from: http://www.arabjpsychiat.com/media/PDF/2011_m/2011_May.pdf

*Feigin, V.L., Barker-Collo, S., Parag, V., Hackett, M.L., Kerse, N., Barber, P.A., . . . Auckland Regional Community Stroke Study Group. (2012). Prevalence and predictors of 6-month fatigue in patients with ischemic stroke: A population-based stroke incidence study in Auckland, New Zealand, 2002-2003. *Stroke, 43*(10), 2604-2609. doi: 10.1161/STROKEAHA.112.660886

*Fuller-Thomson, E., Tulipano, M.J., & Song, M. (2012). The association between depression, suicidal ideation, and stroke in a population-based sample. *International Journal of Stroke, 7*(3), 188-194. doi:10.1111/j.1747-4949.2011.00702.x

*Gainotti, G., Azzoni, A., & Marra, C. (1999). Frequency, phenomenology and anatomical-clinical correlates of major post-stroke depression. *The British Journal of Psychiatry, 175*, 163-167. doi:10.1192/bjp.175.2.163

Glader, E., Stegmayr, B., & Asplund, K. (2002). Poststroke fatigue: A 2-year follow-up study of stroke patients in Sweden. *Stroke, 33,* 1327-1333. doi:10.1161/01.STR.0000014248.28711.D6

Goldberg, D.P. (1972). *The Detection of Psychiatric Illness by Questionnaire*. London: Oxford University Press.

*Greenop, K.R., Almeida, O.P., Hankey, G. J., van Bockxmeer, F., & Lautenschlager, N.T. (2009). Premorbid personality traits are associated with post-stroke behavioral and psychological symptoms: A three-month follow-up study in Perth, Western Australia. *International Psychogeriatrics, 21*(6), 1063-1071. doi:10.1017/S1041610209990457

*Hackett, M.L., & Anderson, C.S. Auckland Regional Community Stroke (ARCOS) Study Group. (2006). Frequency, management, and predictors of abnormal mood after stroke: The Auckland regional community stroke (ARCOS) study, 2002 to 2003. *Stroke, 37*(8), 2123-2128. doi:10.1161/01.STR.0000231387.58943.1f

Hackett, M.L., Anderson, C.S., House, A.O., & Xia, J. (2009). Interventions for treating depression after stroke. *Stroke, 40,* e487-e488. doi:10.1161/STROKEAHA.109.547059

Hackett, M.L., Yapa, C., Parag, V., & Anderson, C.S. (2005). Frequency of depression after stroke: A systematic review of observational studies. *Stroke, 36,* 1330-1340. doi:10.1161/01.STR.0000165928.19135.35

*Haghgoo, H.A., Pazuki, E.S., Hosseini, A.S., & Rassafiani, M. (2013). Depression, activities of daily living and quality of life in patients with stroke. *Journal of the Neurological Sciences, 328,* 87-91. doi:10.1016/j.jns.2013.02.027

Hama, S., Yamashita, H., Shigenobu, M., Watanabe, A., Hiramoto, K., Kurisu, K., . . . Kitaoka, T. (2007a). Depression or apathy and functional recovery after stroke. *International Journal of Geriatric Psychiatry, 22*(10), 1046-1051. doi:10.1002/gps.1866

*Hama, S., Yamashita, H., Shigenobu, M., Watanabe, A., Kurisu, K., Yamawaki, S., & Kitaoka, T. (2007b). Post-stroke affective or apathetic depression and lesion location: Left frontal lobe and bilateral basal ganglia. *European Archives of Psychiatry and Clinical Neuroscience, 257*(3), 149-152. doi:10.1007/s00406-006-0698-7

Hamilton, M. (1960). A rating scale for depression. *Journal of Neurology, Neurosurgery and Psychiatry, 23,* 56-62. Retrieved from http://www.ncbi.nlm.nih.gov/pmc/articles/PMC495331/pdf/jnnpsyc00273-0060.pdf

Higgins, J.P.T., & Deeks, J.J. (2008). Selecting studies and collecting data. In: J.P.T. Higgins & S. Green (Eds.), *Cochrane Handbook for Systematic Reviews of Interventions* (pp.7.2 – 7.28). London: The Cochrane Collaboration. Retrieved from: www.cochrane-handbook.org

*Hilari, K., Northcott, S., Roy, P., Marshall, J., Wiggins, R.D., Chataway, J., & Ames, D. (2010). Psychological distress after stroke and aphasia: The first six months. *Clinical Rehabilitation, 24*(2), 181-190. doi:10.1177/0269215509346090

*Hsieh, L. P., & Kao, H.J. (2005). Depressive symptoms following ischemic stroke: A study of 207 patients. *Acta Neurologica Taiwanica, 14*(4), 187-190. Retrieved from: http://www.ant.org.tw/Mag_Files/14-4/dw20061121542_14-4%20%20p187.pdf

*Hubacher, M., Calabrese, P., Bassetti, C., Carota, A., Stocklin, M., & Penner, I. (2012). Assessment of post-stroke fatigue: The fatigue scale for motor and cognitive functions. *European Neurology, 67*(6), 377-384. doi:10.1159/000336736

*Ingles, J., Eskes, G., & Phillips, S. (1999). Fatigue after stroke. *Archives of Physical Medicine and Rehabilitation, 80*(2), 173-178. doi:10.1016/S0003-9993(99)90116-8

*Kaji, Y., Hirata, K., & Ebata, A. (2006). Characteristics of poststroke depression in Japanese patients. *Neuropsychobiology, 53*(3), 148-152. doi:10.1159/000093340

*King, R.B., Shade-Zeldow, Y., Carlson, C.E., Feldman, J.L., & Philip, M. (2002). Adaptation to stroke: A longitudinal study of depressive symptoms, physical health, and coping process. *Topics in Stroke Rehabilitation, 9*(1), 46–66. Retrieved from: http://thomasland.metapress.com/content/kdtawelct2wrx51w/fulltext.pdf

*Kouwenhoven, S.E., Gay, C.L., Bakken, L.N., Lerdal, A. (2013). Depressive symptoms in acute stroke: A cross-sectional study of their association with sociodemographics and clinical factors. *Neuropsychological Rehabilitation: An International Journal, 23*(5), 658-677. doi:10.1080/09602011.2013.801778

Krupp, L.B., LaRocca, N.G., Muir-Nash, J., & Steinberg, A.D. (1989). The fatigue severity scale: Application to patients with multiple sclerosis and systemic lupus erythematosus. *Archives of Neurology, 46*(10), 1121-1123. doi:10.1001/archneur.1989.00520460115022

*Ku, H., Chen, C., Yang, Y., Hu, C., Wu, D., Chen, C., Chen, P., & Chi, N. (2013). Association between cerebral lesions and emotional changes in acute ischemic stroke patients. *The Journal of Nervous and Mental Disease, 201*(5), 400-406. doi:10.1097/NMD.0b013e31828e0fe9

*Kutlubaev, M.A., Shenkin, S.D., Farrall, A.J., Duncan, F.H., Lewis, S.J., Greig, C.A., Dennis, M.S., Wardlaw, J.M., MacLullich, A.M.J., & Mead, G.E. (2013). CT and clinical predictors of fatigue at one month after stroke. *Cerebrovascular Diseases, 3,* 26-34. doi:10.1159/000347113

*Lam, S.C., Lee, L.Y.K., & To, K.W. (2010). Depressive symptoms among community-dwelling, post-stroke elders in Hong Kong. *International Nursing Review, 57*(2), 269-273. doi:10.1111/j.1466-7657.2009.00789.x

*Lerdal, A., Bakken, L.N., Rasmussen, E.F., Beiermann, C., Ryen, S., Pynten, S., . . . Kim, H.S. (2011). Physical impairment, depressive symptoms and pre-stroke fatigue are related to fatigue in the acute phase after stroke. *Disability and Rehabilitation, 33*(4), 334-342. doi:10.3109/09638288.2010.490867

*Lerdal, A., & Gay, C.L. (2013). Fatigue in the acute phase after first stroke predicts poorer physical health 18 months later. *Neurology, 81,* 1581-1587. doi:10.1212/WNL.0b013e3182a9f471

*Li, S.C., Wang, K.Y., & Lin, J.C. (2003). Depression and related factors in elderly patients with occlusion stroke. *Journal of Nursing Research, 11*(1), 9-18. doi:10.1097/01.JNR.0000347614.44660.b5

*Ligthart, S.A., Richard, E., Fransen, N.L., Eurelings, L.S.M., Beem, L., Eikelenboom, P., . . . Moll van Charante, E.P. (2012). Association of vascular factors with apathy in community-dwelling elderly individuals. *JAMA Psychiatry, 69*(6), 636-642. doi:10.1001/archgenpsychiatry.2011.1858

*Lincoln, N.B., Brinkmann, N., Cunningham, S., Dejaeger, E., De Weerdt, W., Jenni, W., … De Wit, L. (2013). Anxiety and depression after stroke: A 5 year follow-up. *Disability & Rehabilitation, 35*(2), 140-145. doi:10.3109/09638288.2012.691939

*MacHale, S.M., O'Rourke, S.J., Wardlaw, J.M., & Dennis, M.S. (1998). Depression and its relation to lesion location after stroke. *Journal of Neurology, Neurosurgery & Psychiatry, 64*(3), 371-374. Retrieved from: http://jnnp.bmj.com/content/64/3/371.full.pdf

Marin, R.S. (1990). Apathy: A differential diagnosis and classification of apathy. *American Journal of Psychiatry, 147,* 22-30.

Marin, R.S., Biedrzycki, R.C., & Firinciogullari, S. (1991). Reliability and validity of the apathy evaluation scale. *Psychiatry Research, 38,* 143-162.

*Marin, R.S., Firinciogullari, S., & Biedrzycki, R.C. (1994). Group differences in the relationship between apathy and depression. *Journal of Nervous and Mental Disease, 182*(4), 235-239.

McGeough, E., Pollock, A., Smith, L.N., Dennis, M., Sharpe, M., Lewis, S., & Mead, G.E. (2009). Interventions for post-stroke fatigue. *Cochrane Database of Systematic Reviews*. doi:10.1002/14651858.CD007030.pub2

*Mead, G., Graham, C., Dorman, P., Bruins Slot, K., Lewis, S.C., Dennis, M.S. & Sandercock, P.A.G. (2011). Fatigue after stroke: Baseline predictors and influence on survival. Analysis of data from UK patients recruited in the international stroke trial. *PLos ONE, 6(3),* e16988. doi:10.1371/journal.pone.0016988

*Mikami, K., Jorge, R.E., Moser, D.J., Jang, M., & Robinson, R.G. (2013). Incident apathy during the first year after stroke and its effect on physical and cognitive recovery. *The American Journal of Geriatric Psychiatry, 21*(9), 848-854. doi: 10.1016/j.jagp.2013.03.012

Montgomery, S.A., & Asberg, M. (1979). A new depression scale designed to be sensitive to change. *British Journal of Psychiatry, 134,* 382-389. doi:10.1192/bjp.134.4.382

*Murakami, T., Hama, S., Yamashita, H., Onoda, K., Kobayashi, M., Kanazawa, J., Yamawaki, S., & Kurisu, K. (2013). Neuroanatomic pathways associated with poststroke affective and apathetic depression. *The American Journal of Geriatric Psychiatry, 21*(9), 840-847. doi:10.016/j.jagp.2013.01.057

*Naess, H., Lunde, L., & Brogger, J. (2012b). The triad of pain, fatigue and depression in ischemic stroke patients: The Bergen stroke study. *Cerebrovascular Diseases, 33*(5), 461-465. doi:10.1159/000336760

*Naess, H., Lunde, L., Brogger, J., & Waje-Andreassen, U. (2012a). Fatigue among stroke patients on long-term follow-up: The Bergen stroke study. *Journal of the Neurological Sciences, 312*(1-2), 138-141. doi:10.1016/j.jns.2011.08.002

*Naess, H., Nyland, H. I., Thomassen, L., Aarseth, J., & Myhr, K. (2005). Fatigue at long-term follow-up in young adults with cerebral infarction. *Cerebrovascular Diseases, 20,* 245-250. doi:10.1159/000087706

National Institute for Health and Clinical Excellence (NICE). (2008). *Stroke: Diagnosis and initial management of acute stroke and transient ischemic attack (TIA).* (NICE Clinical Guideline 68). London: National Institute for Health and Clinical Excellence.

*Nys, G.M.S., van Zandvoort, M.J.E., van der Worp, H.B., de Haan, E.H.F., de Kort, P.L.M., & Kappell, L.J. (2005). Early depressive symptoms after stroke: Neuropsychological correlates and lesion characteristics. *Journal of the Neurological Science, 228,* 27–33. doi:10.1016/j.jns.2004.09.031

*Okada, K., Kobayashi, S., Yamagata, S., Takahashi, K., & Yamaguchi, S. (1997). Poststroke apathy and regional cerebral blood flow. *Stroke, 28*(12), 2437-2441. doi:10.1161/01.STR.28.12.2437

*Onoda, K., Kuroda, Y., Yamamoto, Y., Abe, S., Oguro, H., Nagai, A., . . . Yamaguchi, S. (2011). Post-stroke apathy and hypoperfusion in basal ganglia: SPECT study. *Cerebrovascular Diseases, 31*(1), 6-11. doi:10.1159/000319771

*Paradiso, S., & Robinson, R.G. (1999). Minor depression after stroke. *The American Journal of Geriatric Psychiatry, 7*(3), 244-251. doi:10.1097/00019442-199908000-00009

*Park, J.Y., Chun, M.H., Kang, S.H., Lee, J.A., Kim, B.R., & Shin, M.J. (2009). Functional outcome in poststroke patients with or without fatigue. *American Journal of Physical Medicine & Rehabilitation, 88*(7), 554-558. doi:10.1097/PHM.0b013e3181a0dae0

*Quaranta, D., Marra, C., & Gainotti, G. (2012). Post-stroke depression: Main phenomenological clusters and their relationships with clinical measures. *Behavioural Neurology, 25*(4), 303-310. doi:10.3233/BEN-2012-110236

*Radman, N., Staub, F., AboulafiaBrakha, T., Berney, A., Bogousslavsky, J., & Annoni, J. (2012). Poststroke fatigue following minor infarcts: A prospective study. *Neurology, 79*(14), 1422-1427. doi:10.1212/WNL.0b013e31826d5f3a

*Raju, R. S., Sarma, P. S., & Pandian, J.D. (2010). Psychosocial problems, quality of life, and functional independence among Indian stroke survivors. *Stroke, 41*(12), 2932-2937. doi:10.1161/STROKEAHA.110.596817

Rickards, H. (2005). Depression in neurological disorders: Parkinson's disease, multiple sclerosis and stroke. *Journal of Neurology, Neurosurgery and Psychiatry, 76* (Supplement 1), i48-i52. doi:10.1136/jnnp.2004.060426

*Rush, B.K., McNeil, R.B., Gamble, D.M., Luke, S.H., Richie, A.N., Albers, C.S., . . . Meschia, J.F. (2010). Behavioral symptoms in long-term survivors of ischemic stroke. *Journal of Stroke & Cerebrovascular Diseases, 19*(4), 326-332. doi:10.1016/j.jstrokecerebrovasdis.2009.09.009

*Santa, N., Sugimori, H., Kusuda, K., Yamashita, Y., Ibayashi, S., & Lida, M. (2008). Apathy and functional recovery following first-ever stroke. *International Journal of Rehabilitation Research, 31*(4), 321-326. doi:10.1097/MRR.0b013e3282fc0f0e

*Schepers, V., Post, M., Visser-Meily, A., van de Port, I., Akhmouch, M., & Lindeman, E. (2009). Prediction of depressive symptoms up to three years post-stroke. *Journal of Rehabilitation Medicine, 41*(11), 930-935. doi:10.2340/16501977-0446

*Schepers, V., Visser-Meily, A.M., Ketelaar, M., & Lindeman, E. (2006). Poststroke fatigue: Course and its relation to personal and stroke-related factors. *Archives of Physical Medicine and Rehabilitation, 87,* 184-188. doi:10.1016/j.apmr.2005.10.005

Schwartz, J.A., Speed, N.M., Brunberg, J.A., Brewer, T.A., Brown, M., & Greden, J.F. (1993). Depression in stroke rehabilitation. *Biological Psychiatry, 33,* 694-699. Retrieved from:

http://deepblue.lib.umich.edu/bitstream/handle/2027.42/30792/0000446.pdf?sequence=1

*Sienkiewicz-Jarosz, H., Milewska, D., Bochynska, A., Chelmniak, A., Dworek, N., Kasprzyk, K., . . . Ryglewicz, D. (2010). Predictors of depressive symptoms in patients with stroke - a three-month follow-up. *Neurologia i Neurochirurgia Polska, 44*(1), 13-20. doi:10.1016/S0028-3843(14)60402-3

*Snaphaan, L., van der Werf, S., & de Leeuw, F. (2011). Time course and risk factors of post-stroke fatigue: A prospective cohort study. *European Journal of Neurology, 18*(4), 611-617. doi:10.1111/j.1468-1331.2010.03217.x

*Starkstein, S.E., Fedoroff, J.P., Price, T.R., Leiguarda, R., & Robinson, R.G. (1993). Apathy following cerebrovascular lesions. *Stroke, 24*(11), 1625-1630. doi:10.1161/01.STR.24.11.1625

*Tang W.K., Chen Y.K., Liang H.J., Chu, W.C.W., Mok, V.C.T., Ungvari, G.S., & Wong K.S. (2013a). Location of infarcts and apathy in ischemic stroke. *Cerebrovascular Diseases, 35*(6), 566-571. doi:10.1159/000351152

*Tang, W.K., Liang, H.J., Chen, Y.K., Chu, W.C.W., Abrigo, J., Mok, V.C.T., . . . Wong, K.S. (2013b). Poststroke fatigue is associated with caudate infarcts. *Journal of the Neurological Sciences, 324*(1-2), 131-135. doi:10.1016/j.jns.2012.10.022

*Tang, W.K., Lu, J.Y., Chen, Y.K., Chu, W.C.W., Mok, V., Ungvari, G.S., & Wong, K.S. (2011). Association of frontal subcortical circuits infarcts in poststroke depression: A magnetic resonance imaging study of 591 Chinese patients with ischemic stroke. *Journal of Geriatric Psychiatry and Neurology, 24*(1), 44-49. doi:10.1177/0891988710392375

*Taylor-Piliae, R.E., Hepworth, J.T., & Coull, B.M. (2013). Predictors of depressive symptoms among community-dwelling stroke survivors. *Journal of Cardiovascular Nursing, 28*(5), 460-467. doi:10.1097/JCN.0b013e318258ad57

*Thompson, S.C., SobolewShubin, A., Graham, M.A., & Janigian, A.S. (1989). Psychosocial adjustment following a stroke. *Social Science & Medicine, 28*(3), 239-247.

*Townend, E., Tinson, D., Kwan, J., & Sharpe, M. (2010). 'Feeling sad and useless': An investigation into personal acceptance of disability and its association with depression following stroke. *Clinical Rehabilitation, 24*(6), 555-564. doi:10.1177/0269215509358934

*Tseng, B.Y., Billinger, S.A., Gajewski, B.J., & Kluding, P.M. (2010). Exertion fatigue and chronic fatigue are two distinct constructs in people post-stroke. *Stroke, 41*(12), 2908-2912. doi:10.1161/STROKEAHA.110.596064

*van de Port, I.G.L, Kwakkel, G., Bruin, M., & Lindeman, E. (2007). Determinants of depression in chronic stroke: A prospective cohort study. *Disability and Rehabilitation: An International, Multidisciplinary Journal, 29*(5), 353-358. doi:10.1080/09638280600787047

van der Werf, S.P., van den Broek, H.L.P, Anten, H.W.M., & Bleijenberg, G. (2001). Experience of severe fatigue long after stroke and its relation to depressive symptoms and disease characteristics. *European Neurology, 45*(1), 28-33. doi:10.1159/000052085

*Vuletic, V., Lezaic, Z., & Morovic, S. (2011). Post-stroke fatigue. *Acta Clinica Croatica, 50*(3), 341-344. Retrieved from: http://www.acta-clinica.kbcsm.hr/arhiva/Acta2011/Acta3/05.pdf

*Weaver, L.L., Page, S.J., Sheffler, L., & Chae, J. (2013). Minimal depression: How does it relate to upper-extremity impairment and function in stroke? *American Journal of Occupational Therapy, 67,* 550–555. doi:/10.5014/ajot.2013.008391

*Winward, C., Sackley, C., Metha, Z., & Rothwell, P.M. (2009). A population-based study of the prevalence of fatigue after transient ischemic attack and minor stroke. *Stroke, 40*(3), 757-761. doi:10.1161/STROKEAHA.108.527101

*Withall, A., Brodaty, H., Altendorf, A., & Sachdev, P.S. (2011). A longitudinal study examining the independence of apathy and depression after stroke: The Sydney stroke study. *International Psychogeriatrics, 23*(2), 264-273. doi:10.1017/S1041610209991116

*Yang, S., Hua, P., Shang, X., Hu, R., Mo, X. & Pan, X. (2013). Predictors of early post ischemic stroke apathy and depression: a cross-sectional study. *BMC Psychiatry, 13,* 164-174. doi:10.1186/1471-244X-13-164

*Zhang, T., Jing, X., Zhao, X., Wang, C., Liu, Z., Zhou, Y., . . . Wang, Y. (2012). A prospective cohort study of lesion location and its relation to post-stroke depression among Chinese patients. *Journal of Affective Disorders, 136*(1-2), e83-e87. doi: 10.1016/j.jad.2011.06.014

*Zhang, W-N, Pan, Y-H, Wang, X-Y, Zhao, Y. (2013). A prospective study of the incidence and correlated factors of post-stroke depression in China. *PLoSONE 8*(11): e78981. doi:10.1371/journal.pone.0078981

Zigmond, A.S., & Snaith, R.P. (1983). The hospital anxiety and depression scale. *Acta Psychiatrica Scandinavica, 67*(6), 361–370.

Section B:

Correlates and Predictors of Apathy, Depression and Fatigue Post-Stroke

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For Submission to 'Stroke'

Abstract

Background and Purpose: Stroke is a leading cause of disability in the UK and has a range of psychological sequelae including apathy, depression and fatigue. Psychological consequences of stroke have been associated with poor rehabilitation outcomes. Apathy, depression and fatigue are often considered to overlap and the research indicates that they may occur both independently and in unison after stroke.

Methods: Sixty-three people aged over 55 years who had a stroke and lived in the community were included in this study. They were assessed using the Apathy Evaluation Scale, Geriatric Depression Scale, the Fatigue Severity Scale and the Barthel index. Socio-demographic data were also collected along with information about their stroke.

Results: 60.3% of participants reached cut-off levels for apathy, 58.7% for depression and 58.7% for fatigue. While there was an overlap in terms of these psychological disorders, they also occurred independently. Physical functioning was the only factor which was related to apathy, depression and fatigue. Apathy was a mediator in the relationship between physical functioning and depression; and depression was a mediator in the relationship between apathy and fatigue. Based on these findings, a significant structural equation model accounting for the relationships between apathy, fatigue, physical functioning and depression was developed.

Conclusions: Apathy, depression and fatigue are common post-stroke. The inter-relationships between these post-stroke sequelae are also related to the person's physical functioning and not to age, side of weakness or time since stroke. Results have implications in terms of the clinical assessment and management of post-stroke psychological sequelae.

Keywords: stroke, apathy, depression, fatigue, Structural Equation Modelling

Stroke is a leading cause of disability in the UK, and occurs when there is a problem with the blood supply to the brain. This can occur due to a blocked blood vessel (ischemic stroke) or a burst blood vessel (haemorrhagic stroke) which results in a lack of oxygen to the brain. One third of people with stroke die, and up to a half of survivors have significant disability as a result (National Audit Office, 2005). These difficulties can include physical, social, emotional and psychological consequences (National Institute for Health and Clinical Excellence [NICE], 2008).

Some of the most common psychological sequelae post-stroke are apathy, depression and fatigue. Prevalence rates for post-stroke apathy have been reported between 15.2 and 71.1%, with a pooled estimate of 36.3% (Caeiro, Ferro & Costa, 2013); rates of depression have been reported between 4 and 63%, with a pooled estimate from studies of 33% (Hackett, Yapa, Parag & Anderson, 2005), and rates for fatigue were reported between 42 and 46% (Duncan, Kutlubaev, Dennis, Greig & Mead, 2012). Apathy, depression and fatigue can have an impact on the person's engagement with rehabilitation programmes and their functional recovery post-stroke (Delaney & Ravdin, 1997; Hama et al., 2007a; Glader, Stegmayr, & Asplund, 2002).

Despite the recognition that psychological consequences of stroke are common and influence recovery post-stroke, treatment guidelines and service provision have historically been poor in providing best practice guidelines and services in the assessment and treatment of mood and tiredness post stroke. The NICE Quality Standard 2 for Stroke (NICE, 2010) outlined that people who have had a stroke should have their mood assessed within 6 weeks of diagnosis. The Sentinel National Stroke Audit (Intercollegiate Stroke Working Party, 2011) reported an improvement in the assessment of stroke patients' mood, prior to discharge from hospital, from 47% in 2004 to 80% in 2010. This indicated a shift in the importance placed on mood and on the adherence to national guidelines when assessing mood of stroke

patients. Despite this, McKevitt et al.'s (2011) UK study of unmet needs of stroke survivors reported that 38.4% reported unmet needs for emotional problems and 51.7% reported unmet needs for fatigue.

While there are recommendations in place in terms of assessment of mood, there are not clear treatment guidelines for psychological consequences of stroke. The NICE Guidelines on Stroke Rehabilitation (NICE, 2013, p.35) outlined how there is not 'robust evidence' for the effectiveness of different psychological treatments for people post-stroke. This guideline recommends that the NICE 91 guideline (NICE, 2009) on 'Depression in Adults with Physical Health' is followed in the management of post-stroke depression. This guideline proposes a 'stepped care' model where people with low levels of depression are provided with education, working up to group cognitive behaviour therapy (CBT), individual CBT and other psychosocial interventions and a combination with anti-depressants if required, for people with moderate and severe depression. The National Clinical Guidelines for Stroke (Intercollegiate Stroke Working Party, 2012) outlined how a biopsychosocial model can be useful in considering psychological care post-stroke.

The biopsychosocial model of understanding health and disease was proposed by Engel (1977) as an alternative to using a biomedical model and as such it includes social and psychological factors as well as medical and biological factors in considering the person who has a health issue. Given that research has indicated that both neuroanatomical / organic factors as well as reactive factors have been related to post-stroke depression, it seems fitting that a holistic model of healthcare is adopted in order to understand the psychological consequences of stroke.

As outlined, apathy, depression and fatigue are commonly reported post-stroke. Reports from the literature indicated that while they may overlap post-stroke, that they can also occur independently (Onoda et al., 2011; Tang et al., 2013), which has implications in

terms of the assessment, management and treatment of people experiencing psychological issues post-stroke. To date, there has been no original research looking at apathy, depression and fatigue together, nor has there been any original research looking at the relationships between apathy and fatigue. Although there have been many reports in the literature about the relationship between apathy and depression, there are conflicting reports as to whether or not they are related. Two studies using regression models have indicated that depression is a significant predictor of apathy (Brodaty, Liu, Withall and Sachdev, 2013; Yang et al., 2013), while two have reported that there was not a significant relationship (Caeiro, Ferro & Figueira, 2012; Caeiro, Ferro, Pinho e Melo, Canhão & Figueira, 2013). There did appear to be a body of evidence to indicate that there was a significant relationship between depression and fatigue in stroke survivors (Snaphaan, van der Werf & de Leeuw, 2011; van de Port, Kwakkel, Bruin & Lindeman, 2007).

A range of factors have been identified which are related to post-stroke apathy, depression and fatigue. In terms of apathy, there was evidence for a link with the basal ganglia (Hama et al., 2007b), poorer physical functioning (Tang et al., 2013) and older age (Brodaty et al., 2005; Yang et al., 2013). In terms of depression, there was strong evidence for significant relationships with poorer physical functioning (Carota et al., 2005; Naess, Lunde & Brogger, 2012), female gender (Dam, 2001; Haghgoo, Pazuki, Hosseini & Rassafiani, 2013), pre-stroke depression (Hackett & Andersen, 2006; Taylor-Piliae, Hepworth & Coull, 2013), lack of social support (Lam, Lee & To, 2010; Taylor-Piliae et al., 2013) and stroke severity (Tang et al., 2011). In terms of fatigue, there was evidence for significant relationships with poorer physical functioning (Appelros, 2006; Lerdal et al., 2011) and female gender (Kutlubaev et al., 2013; Lerdal et al., 2011). Common predictors of apathy, depression and fatigue therefore included poorer physical functioning, female gender and increased severity of stroke.

Research to date indicated that post-stroke apathy and fatigue were more influenced by biological factors, such as lesion location, poorer physical functioning, gender and age; whereas depression was related to biological, psychological and social factors. This supports a theoretical framework of a biopsychosocial model in understanding psychological sequelae of stroke.

The current study aimed to explore the relationships between apathy, depression and fatigue post-stroke, in an attempt to better understand how these factors interact post-stroke. It further aimed to identify any significant biological and social confounders within these relationships.

With advances in healthcare treatments, more people are surviving stroke; this combined with the ageing population has led to an increase in people who have survived a stroke, and who are living with the psychological consequences. As such, it is timely to investigate the inter-relationships between psychological sequelae of stroke and the other biological and social factors which may influence these relationships.

Clinically, having a better understanding of these inter-relationships, will allow for recommendations in terms of the assessment, management and treatment of people post-stroke. As apathy, depression and fatigue can impact on engagement in rehabilitation and rehabilitation outcomes, having a better understanding of these constructs may have an impact on the work of members of the multi-disciplinary team in providing care to people post-stroke.

Aims

This study aimed to examine the inter-relationships between apathy, depression and fatigue post-stroke; and to identify any common predictors of these three constructs.

Hypotheses

a. A number of factors including location of stroke, time since stroke, stroke severity, gender, age and history of psychiatric illness will be related to the presence of 1) apathy, 2) depression and 3) fatigue.

b. There will be significant positive relationships between

i. apathy and depression,

ii. apathy and fatigue,

iii. depression and fatigue,

iv. apathy, depression and fatigue,

and these will be associated with common significant predictor variables such as time since stroke, stroke severity, gender, age and history of psychiatric illness.

Method

Participants

Participants were 63 men and women aged over 55 years who ever had a stroke. They were recruited through NHS stroke services and local charities in East Kent and through national charities providing support to people with stroke. People were included if they had ever had a stroke and were aged over 55 years, could provide written consent or complete a written questionnaire, and English was their first language, or they could indicate that they lived in the UK for a prolonged period of time indicating that they could understand the questions provided in English. Exclusion criteria were if people had a transient ischaemic attack (TIA) and not a stroke.

Design

A cross-sectional design was used. The study was a postal questionnaire and information was provided by the person who had a stroke; they were provided with the option to seek help from a family member or carer with completing the questionnaires if required.

Procedure

Ethical Considerations & Ethics. Participants were recruited from the community and not in the acute phase post-stroke. This was in order to minimise any further distress to people who have recently experienced a stroke. Given that people were completing personal information and returning it by post, this was protected by providing people with two prepaid envelopes in order to return their consent form separately to their data, so as to ensure their anonymity if any documents were lost in the post. Consent forms were stored separately to the response booklets in locked cabinets in the clinical psychology programme office. These will be held in paper form until the study is completed. Data from the response booklets were transferred to electronic form and stored securely on a password protected device. This will be held by the researcher for 10 years after study completion. It was deemed that by participating in the research, people were not subjected to any added distress than that encountered in routine care.

The study received favourable ethical approval from London Queens Square Research Ethics Committee (REC; see Appendix C). Local approval to recruit through NHS stroke services in East Kent was received from the Research Management & Governance Consortium for Kent and Medway (see Appendix D). Permission was gained from a number of charities, who provide services to people who have had a stroke, to distribute information packs to their members. Charities included East Kent Strokes, Headway and the Stroke Association. The study followed the British Psychological Society's (BPS; 2011) Code of Human Research Ethics.

Recruitment. Questionnaires were provided to local NHS stroke services through Intermediate Care Teams in East Kent and local charities providing support to people with stroke. The study was also advertised on national charity websites providing support to people with stroke (Headway and Stroke Association). Staff in the services provided the information

pack (see Appendix E for participant information sheet) and questionnaires, together with prepaid return envelopes, to people who met the criteria for the study. Those recruited through websites were sent the information pack and questionnaires directly by the researcher. Participants returned completed anonymised questionnaires and a consent form (see Appendix F) separately by post to the research team. Where consent forms were not returned by post, but response booklets were, consent was presumed. This was in line with ethical approval (see Appendix G Substantial Amendment 2).

Assessments. Standardised assessments of apathy, depression, fatigue and physical functioning were used, along with a socio-demographic questionnaire which also gained some history about the person's stroke, education, employment and living arrangements (see Appendices I - M). The standardised assessments used have all been validated for use with a stroke population.

The Apathy Evaluation Scale – Self Report (AES-S; Marin, Biedrzycki & Firinciogullari, 1991) was used to assess apathy (see Appendix I). The AES-S is a self-report measure which comprises of 18 items, asking about the person's interest and motivation in the last four weeks. Respondents reply on a 4-point Likert scale. Total scores range from 18-72, with higher scores indicating more apathy. The AES was developed for use with people who have had a stroke and as such purports to be an accurate measure of apathy in people with stroke. It has an internal consistency of .86; test-retest reliability of .76; and discriminant validity with the Zung Rating Scale for Depression (Zung, 1965) of .42 (Marin et al., 1991). This score (.42) is less than the .85 recommended to determine that two assessment tools are measuring distinct constructs.

The Geriatric Depression Scale (GDS; Yesavage et al., 1983) was used to assess depression (see Appendix J). The GDS comprises of 30 items which are answered yes / no and asks respondents to score their answers based on how they felt in the past week. Scores range

from 0 – 30 and can be categorised into mild / no depression (scores from 0 – 9), moderate depression (scores from 10 – 19) and severe depression (scores 20-30). It has been developed for use with older people and unlike some other measures of depression it does not include items asking about worry about health or appearance, which may be biased in a sample of older people. In stroke patients, it has an internal consistency of .89; test-retest reliability of .75 (Sivrioglu et al., 2009); and concurrent validity with the Center for Epidemiologic Studies Depression Scale (CES-D; Eaton, Muntaner, Smith, Tien & Ybarra, 2004) of .82 (Agrell & Dehlin, 1989).

The Fatigue Severity Scale (Krupp, LaRocca, Muir-Nash & Steinberg, 1989) was used to assess fatigue (see Appendix K). This scale comprises of 9 items asking about fatigue and its impact. Items are scored on a 7 point Likert scale depending on how much / how little the respondent agrees with the statement, thinking about the past week. Total scores range from 9 – 63, with higher scores indicating increased levels of fatigue. It has an internal consistency between .88 and .95; and test-retest reliability of .84 (Whitehead, 2009).

The Barthel Index (Mahoney & Barthel, 1965) is a commonly used standardised assessment of physical functioning (see Appendix L) and asks about the person's ability to do 10 tasks, such as feeding and mobility. Total scores range from 0 – 100 with higher scores indicating more independence. In stroke patients, it has an internal consistency of .84; and concurrent validity of .92 with the Functional Independence Measure, another widely used measure of physical functioning (Hsueh, Lin, Jeng & Hsieh, 2002).

Overall, these scales are reliable and valid assessments of apathy, depression, fatigue and physical functioning in people who have had a stroke.

Statistical Analysis & Sample Size

Based on the literature, nine potential predictor variables of apathy, depression and fatigue were identified, including apathy / depression / fatigue, physical functioning, time since

stroke, number of strokes, gender, side of weakness / lesion, age and history of mental ill-health. Using a regression model with nine predictor variables, a sample size of 113 was required in order to see a medium effect size of .15 with Type I error of 5% and 80% power. Analyses were performed using PASW v.21 and AMOS v.21. Tests were two-tailed with significance at $p = < .05$.

Descriptive statistics provided frequencies of apathy, depression and fatigue in the sample. Univariate analyses were used to assess the relationships between the three outcome variables (apathy, depression and fatigue) and possible confounding variables identified from the literature. Linear multiple regression models were used to analyse the predictors of apathy, depression and fatigue separately. Predictor variables were identified from the univariate analyses and were adjusted for in the regression models.

Based on the findings from the regression models, Structural Equation Modelling (SEM) was used to investigate the relationships between apathy, depression and fatigue, and significant predictor variables. Using this approach a theoretical model to understand the relationships between these variables was developed.

Results

Response Rate

A total of 384 packs were provided to recruiting sites to distribute to potential participants; of these 73 were returned, representing a 19% response rate. Ten were excluded as they did not meet the criteria for inclusion in the study (all due to having an age below 55 years). Valid replies represented a response rate of 16%. A review by Asch, Jedrziewski and Christakis (1997) indicated that the average response rate to postal questionnaires in a patient sample was 60%. The response rate in the current study was therefore lower than expected.

Participant Characteristics

Participants in the current study included 63 people (34 men and 28 women), mean age 71.8 (SD = ± 9.5) years at an average of 53.89 (SD = ± 66.29) months post stroke. The demographics of the participants are shown in Table 1.

Table 1
Participant Demographics

		n
Age (Years)	Range: 55 - 91 $\overline{x}$ = 71.8; SD = 9.5	59
Gender		62
Male	54.8%	
Female	45.2%	
Education		
Secondary level completed	62.3%	38
Third level completed	37.7%	23
Time since stroke (Months)	Range: 1 - 364 $\overline{x}$ = 53.89; SD = 66.29	63
Number of strokes		
Had 1 stroke	82.5%	52
Had 2 strokes	9.5%	6
Had 3 strokes	6.3%	4
Had 4 strokes	1.6%	1
Side of weakness		
Right	49.2%	31
Left	39.7%	25
Neither right nor left	11.1%	7
History of MH problem	6.3%	4
Previous diagnosis of depression	6.3%	4
History of physical health problems	77.8%	49
Pre-stroke diabetes	15.9%	10
Pre-stroke fatigue	9.75%	6
Pre-stroke heart disease	12.7%	8
Pre-stroke hypertension	38.1%	24
Pre-stroke TIA	14.3%	9
Pre-stroke ABI	1.6%	1
Pre-stroke neurological conditions	7.9%	5
Self-rated health at time of stroke		
Excellent	20.6%	13
Good	54%	34
Fair	17.5%	11
Poor	7.9%	5
Marital status		
Married	53.2%	33
Single / never married	6.5%	4
Divorced	16.1%	10
Widowed	24.2%	15

Standardised Assessment Scores

The main outcome measures, apathy, depression and fatigue were all normally distributed (see Appendix N). Scores from the Barthel index were not normally distributed. It had a skewness of -1.21, with a standard error of .3. Scores on the Apathy Evaluation

Scale ranged from 21 – 63, with a mean of 36.86 (SD = 10.96) and 60.3% (n = 38) reaching clinical cut off scores for apathy. This was using a cut-off score of 34 as proposed by Andersson, Krogstad & Finset (1999) in a sample of people with acquired brain injury. Scores on the Geriatric Depression Scale ranged from 0 - 28, with a mean of 12.08 (SD = 7.79). Of the 63 participants, 41.3% had scores within the normal range for depression (n = 26), 38.1% self-reported mild levels of depression (n = 24) and 20.6% of respondents had severe depression (n = 13). These cut off levels were provided within the GDS (Yesavage et al., 1983). Fatigue Severity Scale scores ranged from 9 - 63, with a mean of 38.63 (SD = 15.11) and 58.7% reached clinical cut-off scores for fatigue (n = 37). A cut off of 36 was used to indicate fatigue or no fatigue, as outlined by Krupp et al. (1989). The Barthel index scores ranged from 20-100, with a mean of 82.5 and median score of 90.

Relationships between Apathy, Depression, Fatigue and Barthel scores

Correlations. Apathy was significantly associated with depression ($r = .72$; $p < .001$), fatigue ($r = .47$; $p < .001$) and the Barthel ($r = -.53$; $p < .001$). Depression was significantly associated with apathy ($r = .72$; $p < .001$), fatigue ($r = .57$; $p < .001$) and the Barthel ($r = -.47$; $p < .001$). Fatigue was significantly associated with apathy ($r = .47$; $p < .001$), depression ($r = .57$; $p < .001$) and the Barthel ($r = -.25$; $p = 0.049$).

Partial Correlations. A first order partial correlation between apathy and depression, controlling for fatigue was conducted and showed a moderate correlation ($r = .62$; $p < .001$). This indicated that fatigue reduced the strength of relationship between apathy and depression as without controlling for fatigue, there was a strong relationship observed ($r = .72$; $p < .001$).

First order partial correlation between apathy and fatigue, controlling for depression showed a weak relationship ($r = .1$; $p = .44$). This indicated that the relationship between apathy and fatigue is reduced to no significance once depression is controlled for; without controlling for

depression a moderate relationship was observed ($r = .47$; $p < .001$). First order partial correlation between fatigue and depression, controlling for apathy showed a moderate relationship ($r = .38$; $p = .002$). Again this was a reduction in the extent of the relationship between depression and fatigue, when apathy was not accounted for, when a moderate relationship with a higher correlation co-efficient was observed ($r = .57$; $p < .001$).

Differences between groups. When groups were split into those who had depression ($n = 37$) and those who did not ($n = 26$), and the relationships between apathy and fatigue were examined in these groups separately, the relationship was not significant in either group. A weak non-significant relationship between apathy and fatigue was seen in both the depressed ($r = .25$; $p = .14$) and non-depressed groups ($r = .34$; $p = .09$).

Based on a scatterplot (see Appendix O), it seemed that the relationship between apathy and depression was slightly stronger in those who were fatigued, compared to those who were not fatigued. When groups were split and the correlations were carried out separately for those who were fatigued ($n = 37$) and those who were not ($n = 26$), there were still significant correlations between depression and apathy in both groups. For those with fatigue a strong correlation was observed ($r = .7$; $p < .001$) while for those without fatigue a moderate relationship was observed ($r = .57$; $p < .001$).

Relationships between Apathy, Depression, Fatigue and other variables

As mentioned in the introduction to this work, a number of potential factors which may be related to apathy, depression and fatigue have been identified in the literature. The relationships between apathy, depression and fatigue and these variables were analysed in the current study. Variables included the following:

- age;
- gender;
- education;

- time since stroke;
- number of strokes;
- side of weakness;
- previous mental health diagnosis;
- physical health conditions pre-stroke;
- self-rating of general health and
- marital status.

Results from these analyses indicated that there were no significant relationships observed between apathy, depression and fatigue and any of the variables, with the exception of previous mental health diagnosis. Apathy scores were significantly higher in those who had a previous diagnosis of mental health, compared to those who had not had a previous diagnosis ($t = -2.16$; $df = 61$; $p = .04$).

Relationships between the Other Variables

In order to identify if there were any potential interactions between potential confounders in the relationships between apathy, depression and fatigue, relationships between these variables were analysed. Significant relationships were observed between a number of these factors. In terms of age, widowed participants were significantly older than the other groups within marital status ($F = 6.79$; $df = 3$; $p < .001$). In terms of education, there were significant relationships observed on chi-square tests between education (secondary versus third level education completed) and self-rated health; and on t-test with time since stroke. Those with lower education level were more likely to self-rate their health as lower than those with higher education levels ($\chi^2 = 10.57$; $df = 3$; $p = .014$). Those people with third level education had a significantly longer time since their stroke than those in secondary education ($t = -2.86$; $df = 25.12$; $p = .008$). However, the numbers in the cells were small and these findings are unlikely to be interpretable. In terms of number of strokes,

there was a significant relationship between number of strokes and having a previous mental health diagnosis and physical health condition. Those people with a previous mental health diagnosis were significantly more likely to have had a greater number of strokes ($t = -2.9$; $df = 61$; $p = .005$). Those who had a previous medical condition were also significantly more likely than those who had not to have had a greater number of strokes ($t = -2.04$; $df = 59.49$; $p = .046$). No other significant relationships were observed between these variables.

Summary. There were significant relationships observed between education level and time since stroke; education level and self-rated health; marital status and age, with those who were widowed older than any of the other groups; number of strokes and physical health; and number of strokes and previous mental health diagnosis. However, given the small numbers in some of these groups (those with previous mental health diagnosis; in marital status groups) these findings need to be interpreted with caution. Based on these analyses, it is likely that the potential confounding variables in the relationships between apathy, depression and fatigue are largely independent.

Multiple Regression

Apathy. Multiple linear regressions were conducted to develop a model for predicting apathy from depression and fatigue. Based on the univariate analyses reported earlier, adjustments were made for variables with significant relationships with apathy, including the Barthel score and pre-stroke mental health diagnosis. Results were presented as standardised β-coefficients and confidence intervals (CIs) and are presented in Table 2.

Table 2

Predictors of Apathy

Variable	**Model 1**		**Model 2**		**Model 3**		**Model 4**	
	β	**95% CI**	**β**	**95% CI**	**β**	**95% CI**	**β**	**95% CI**
Constant	24.74	[21.1, 28.38]	23.22	[17.77, 28.68]	36.51	[24.76, 48.26]	29.97	[15.01, 44.93]
Depression	.72**	[.76, 1.26]	.67**	[.63, 1.25]	.55**	[.44, 1.09]	.53**	[.43, 1.07]
Fatigue			.09	[-.09, .22]	.09	[-.09, .22]	.09	[-.08, .22]
Barthel					-.25*	[-.25, -.03]	-.23*	[-.24, -.02]
Previous mental health diagnosis							.12	[-2.26, 13.32]
R^2	.51		.52		.57		.58	
F	63.24**		31.67**		24.17**		19.68**	
ΔR^2			.005		.05		.01	
ΔF			.56		6.39*		1.95	

* $p < .05$ ** $p < .01$

β = Unstandardised β co-efficient CI = Confidence Interval

These regression models indicated that a significant model looking at predictors of apathy found that depression and physical functioning, as measured by the Barthel, were both significant predictors of depression and accounted for 58% of the variance in apathy scores. Fatigue was not a significant predictor of apathy in this model.

Depression. Multiple linear regressions were conducted to develop a model for predicting depression from apathy and fatigue. Based on the univariate analyses reported earlier, adjustments were made for the Barthel, which was the only factor which was significantly related to depression. Results are presented in Table 3.

Table 3
Predictors of Depression

Variable	**Model 1**		**Model 2**		**Model 3**	
	β	**95% CI**	**β**	**95% CI**	**β**	**95% CI**
Constant	-6.72	[-11.65, -1.8]	-9.08	[-13.9, -4.27]	-3.15	[-13.5, 7.19]
Apathy	.72**	[.38, .64]	.58**	[.27, .54]	.36**	[.21, .51]
Fatigue			.3**	[.06, .25]	.16*	[.06, .25]
Barthel					-.05	[-.13, .03]
R^2	.51		.59		.59	
F	63.24**		41.68**		28.66**	
ΔR^2			.07		.01	
ΔF			10.31**		1.68	

* $p < .05$ ** $p < .01$
β = Unstandardised β co-efficient CI = Confidence Interval

These regression models indicated that a significant model looking at predictors of depression found that apathy and fatigue were both significant predictors of depression and accounted for 59% of the variance in depression scores. The Barthel score was not a significant predictor of depression in this model.

Fatigue. Multiple linear regressions were conducted to develop a model for predicting fatigue from apathy and depression. Based on the univariate analyses reported earlier, adjustments were made for the Barthel, which was the only factor which was significantly related to fatigue. Results are presented in Table 4.

Table 4
Predictors of Fatigue

Variable	Model 1		Model 2		Model 3	
	β	**95% CI**	**β**	**95% CI**	**β**	**95% CI**
Constant	25.33	[19.43, 31.23]	21.43	[9.47, 33.4]	16.41	[-9.41, 41.92]
Depression	.57**	[.7, 1.51]	.49**	[.36, 1.53]	.5**	[.37, 1.56]
Apathy			.44	[-.25, .58]	.14	[-.25, .63]
Barthel					.06	[-.15, .24]
R^2	.33		.33		.33	
F	29.05**		14.7**		9.74**	
ΔR^2			.006		.002	
ΔF			.56		.2	

* $p < .05$ ** $p < .01$
β = Unstandardised β co-efficient CI = Confidence Interval

These regression models indicated that a significant model looking at predictors of fatigue found that depression was the only significant predictor of fatigue, accounting for 33% of the variance.

Correlates and Predictors of Apathy, Depression and Fatigue Post-Stroke

Based on correlations, it would seem that apathy, depression and fatigue are related post-stroke. However, looking at partial correlations indicated that the relationship between these constructs may be more complex, as the significant relationship between apathy and depression disappears once fatigue is accounted for, indicating that fatigue may play a mediating role in this relationship.

Looking at the regression models indicated that the best model to explain variances in scores was a model predicting depression which accounted for 59% of the variance in depression scores. Significant predictors in this model included apathy and fatigue. Once the Barthel was accounted for in this model, the model was no longer significant and adjusting for the Barthel did not account for any increase in the variance in depression scores.

The role of gender. In order to explore if relationships between apathy, depression, fatigue and the Barthel were different across gender, separate analyses were performed for men and women. Apathy and depression; apathy and the Barthel; and depression and the Barthel were significantly correlated in both men and women separately.

In men, fatigue was significantly related to depression ($r = .74$; $p < .001$), but not in women ($r = .34$; $p = .08$). In men, fatigue was significantly related to apathy ($r = .61$; $p < .001$), but not in women ($r = .295$; $p = .13$). In men, fatigue is significantly related to Barthel score ($r = -.46$; $p = .008$), but not in women ($r = -.03$; $p = .89$). Based on these findings it seemed that post-stroke fatigue played a more important role for men than for women.

Structural Equation Modelling

Mediating factors.

Depression as a mediator of apathy and fatigue. The partial correlation conducted between apathy and fatigue controlling for depression indicated that depression may be a mediator in this relationship. The significant moderate relationship between apathy and fatigue ($r = .47$; $p < .001$) was reduced to a weak non-significant correlation ($r = .1$; $p < .44$) once depression was controlled for. A Structural Equation Model (SEM) was conducted in order to test if depression was a mediator in the relationship between apathy and fatigue. This resulted in a significant model (see Figure 1) which indicated that depression was a mediator between apathy and fatigue ($\chi^2 = .62$; $df = 1$; $p = .43$). There are a number of other ways to establish the fit of a SEM model including assessing the minimum discrepancy between models, taking account of the degrees of freedom (CMIN/DF). A value of 1 indicates a good fit, while a value between 1 and 2 indicates an acceptable fit. Another assessment of fit is the comparative fit index (CFI), where a value of 0 indicates poor fit, > .95 indicates a good fit, and nearer to 1 indicates a very good fit. A further assessment of fit is the root mean square error of approximation (RMSEA), where a score of 0 is an exact or good fit, and a score < .05 indicates good fit (Byrne, 2001). In this model, all of these indicated a good fit (CMIN/DF = .62; CFI = 1, and RMSEA was <.001).

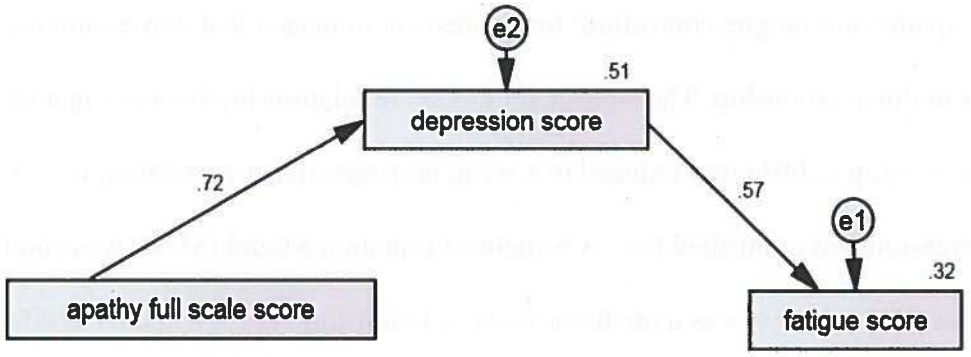

Figure 1 Depression as mediator of apathy & fatigue

Apathy as a mediator of depression and the Barthel. As the regression model which predicted depression from apathy, depression, fatigue and the Barthel was not significant; but correlations between depession and the Barthel were significant ($r = -.47$; $p < .001$), a SEM was conducted to test if apathy was a mediating factor in the relationship between depression and the Barthel.

As mentioned earlier the Barthel scores were not normally distributed. In order to conduct SEM, it is necessary for all variables to be normally distributed. Log transformations were undertaken in order to attempt to adjust for this in the Barthel scores. These transformations resulted in further skew in the Barthel scores and did not result in a normal distribution, as such it was decided to use the original non-transformed Barthel scores in the analyses. There has been some debate over how valid a model is when data is not normally distributed. However, all efforts were made to transform the data but did not reach a significantly normal distribution for the Barthel scores.

The model (see Figure 2) looking at apathy as a mediator between depression and the Barthel was significant ($\chi^2 = 1.55$; $df = 1$; $p = .21$). Two of the indicators of fit suggested that this model was a good fit (CMIN/DF = 1.55; CFI = .99), however, the RMSEA of .09 indicated that the model was not a good fit. Taken together, it can be postulated that this model was a good fit for the data.

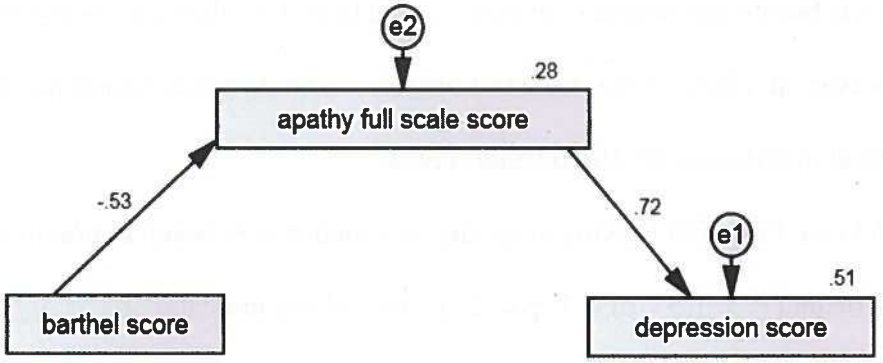

Figure 2 Apathy as mediator of physical functioning and depression

Both of these models were run separately for males and females and both resulted in significant models. While the extent of relationships was different between males and females, overall the model still fitted for males and females separately. This indicated that there was not a mediating moderating effect of gender in these models.

Fatigue as a mediator of depression and the Barthel. As the regression model which predicted depression from apathy, depression, fatigue and the Barthel was not significant; but correlations between fatigue and the Barthel were significant ($r = -.25$; $p = .049$), a SEM was conducted to test if fatigue was a mediating factor in the relationship between depression and the Barthel. This model was not computable indicating that fatigue was not a mediator of the relationship between depression and the Barthel.

Structural Equation Modelling of Depression

A SEM model was conducted to look at the relationships between apathy, depression, fatigue and the Barthel scores. The results from the correlation analyses indicated that apathy, depression, fatigue and Barthel are related post-stroke. The regression models suggested that the highest level of variance in scores was predicted in depression scores (59%) in a model where apathy and fatigue were significant predictors of depression. Adding the Barthel to this model did not result in any increase in the variance explained. Based on these findings a SEM model accounting for the Barthel, apathy, depression and fatigue was proposed (see Figure 3). This model was significant ($\chi^2 = 1.75$; $df = 1$; $p = .19$), and accounted for 58% of the variance in depression scores. Two of the indices of fit indicated that the model was a good fit (CMIN/DF = 1.75; CFI = .99), however, the RMSEA did not indicate a good fit (RMSEA = .11). Taken together, it can be postulated that this model was a good fit.

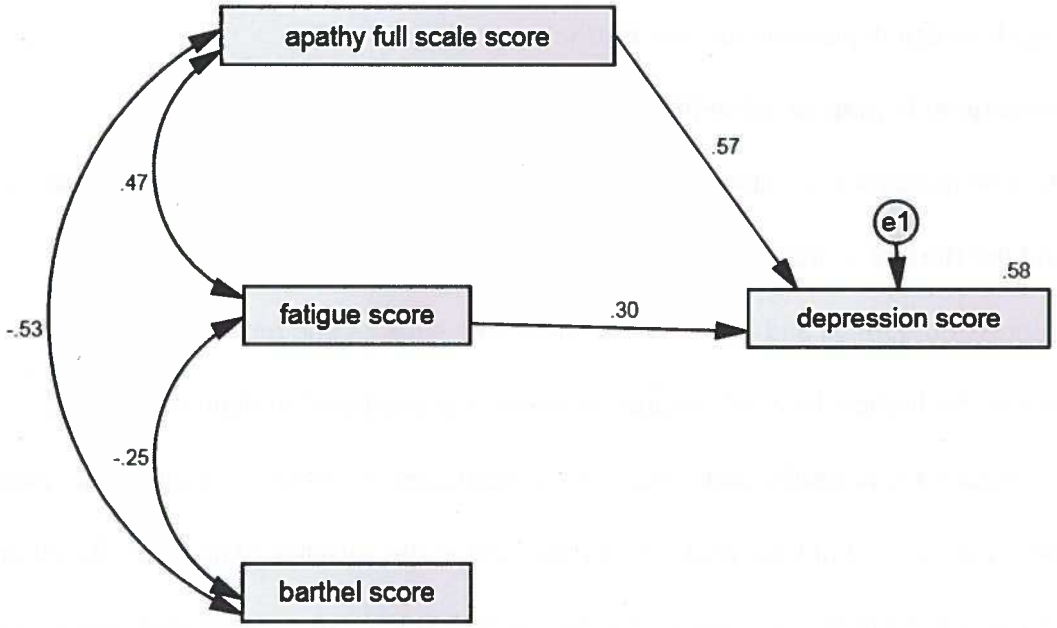

Figure 3 Relationships between apathy, fatigue, physical functioning & depression

The role of gender. In order to see if this model was significant for both men and women, separate SEM models were conducted for men and women.

In men. A SEM model using the same proposed model as before was conducted for men (see Figure 4). The model was significant ($\chi^2 = .63$; df = 1; p = .43). All indicators of fit suggested that this model was a good model for men (CMIN/DF = .63; RMSEA = .00; CFI = 1). There's a difference in this model for men than in the overall sample, as the covariance between the Barthel and fatigue is significant in this model, where it was not when men and women were included.

In women. The SEM model was conducted separately for women (see Figure 5) and was significant ($\chi^2 = .31$; df = 1; p = .58). Similar to the situation with men, all indicators of fit of this model were good (CMIN/DF = .31; RMSEA = .00; CFI = 1).

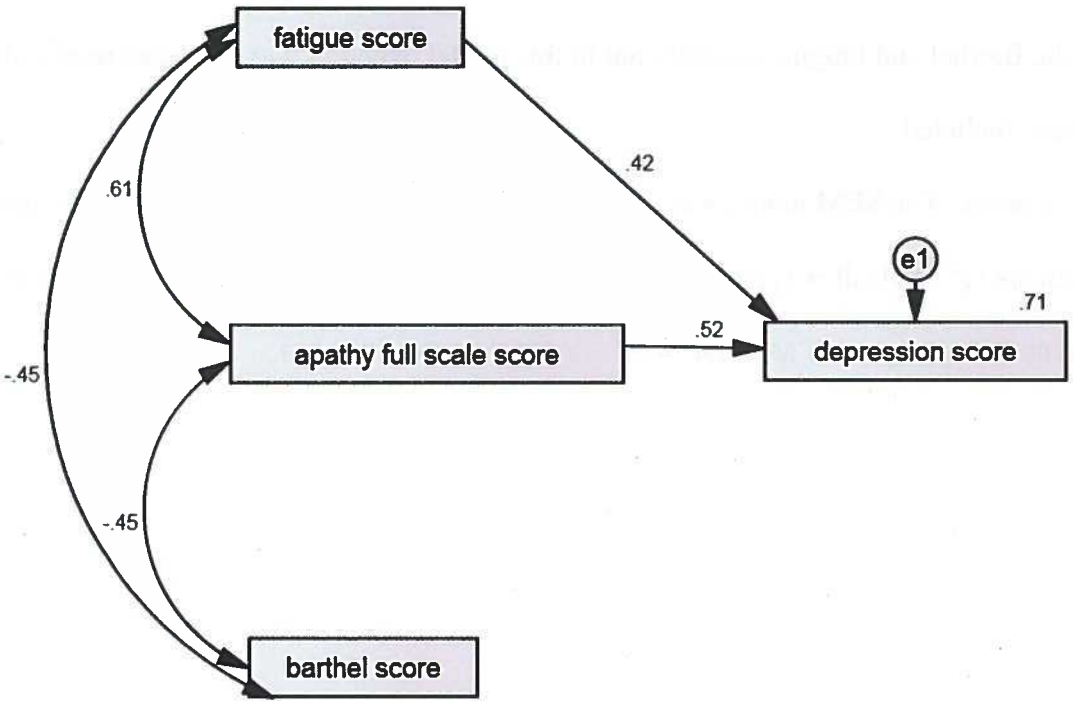

Figure 4 Relationships between apathy, fatigue, physical functioning and depression in men

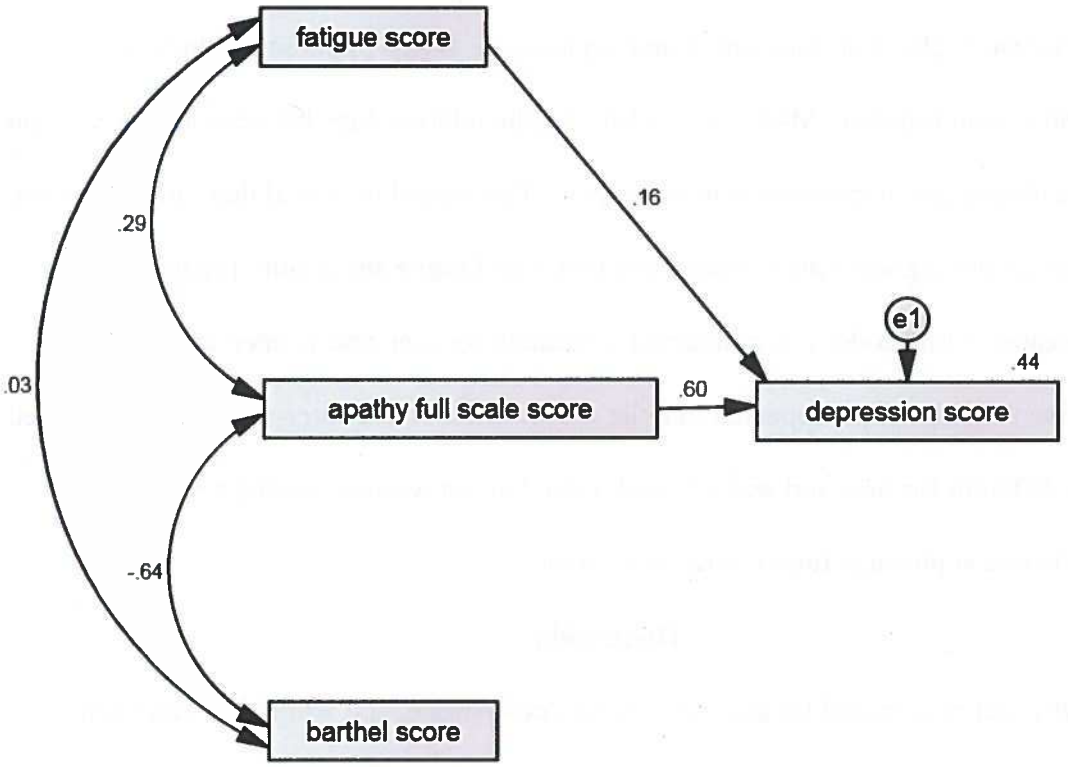

Figure 5 Relationships between apathy, fatigue, physical functioning and depression in women

Summary of Results

Of the participants in the current study, 60.3% reached cut-off levels for apathy, 58.7% for moderate / severe depression and 58.7% for fatigue. While there was an overlap in terms of these three psychological disorders, they also occurred independently. Physical functioning was the only factor which was related to apathy, depression and fatigue. Depression was a mediator in the relationship between apathy and fatigue; and apathy was a mediator in the relationship between physical functioning and depression. Based on these findings, a significant Structural Equation Model accounting for the relationships between apathy, fatigue, physical functioning and depression was developed. This model indicated that fatigue, apathy and physical functioning were inter-related and that both fatigue and apathy predicted post-stroke depression. This model was conducted separately for men and women and while the model remained significant, it appeared that the way in which these inter-relationships worked was slightly different for men and women, with men, but not women, having a significant relationship between physical functioning and fatigue.

Discussion

Apathy, depression and fatigue are common post-stroke, and while they can occur independently, there is often overlap in their presentation, with people experiencing two or more of these psychological consequences of stroke. The relationship between apathy and fatigue is mediated by depression. Previous research has outlined the relationships between apathy and depression post-stroke, and between fatigue and depression post-stroke; however to date there has been no research which looks at these three constructs together. The current research identified the role of physical functioning in the inter-relationships between apathy, depression and fatigue post-stroke. While previous research has identified the role of physical functioning in predicting apathy, depression and fatigue post-stroke, to date there has not been a model which accounts for physical functioning in the inter-relationships between apathy,

depression and fatigue. Unlike previous research, the current study did not identify any social factors, such as education, employment or marital status which related to depression, apathy or fatigue. While this was the case, it seems likely that social factors may also account for some of the psychological issues experienced by people with stroke; although this may be more linked to the management of these issues rather than their development post-stroke. Unlike previous research, the current study also did not identify any role for the side of weakness, indicative of brain lateralisation, in the development of apathy, depression and / or fatigue post-stroke. However, given the role of physical functioning in these inter-relationships, it seemed likely that a biopsychosocial model can be applied when considering the assessment and treatment of psychological sequelae of stroke.

The results from the current study indicated that physical functioning was a significant predictor of apathy in regression models, but not for depression or fatigue. Given that apathy was a significant mediator of the relationship between physical functioning and depression, it appeared that the relationship between apathy and physical functioning plays an important role in post-stroke depression. The SEM model also indicated a strong relationship between physical functioning and apathy. It can by hypothesised that people with significantly more physical impairments have more apathy and that this may lead to a vicious cycle where having physical restrictions leads to a lack of motivation which in turn leads to greater problems with physical functioning and the development of post-stroke depression. While fatigue was not a significant predictor of apathy, there was a strong correlation observed between these two constructs. It seems likely that for people with difficulties with post-stroke fatigue that this will be related to reduced motivation and the subsequent development of depression. Further prospective studies would be beneficial in testing these hypotheses to look at the timeline of the development of these post-stroke sequelae.

It is of interest that the inter-relationships between apathy, depression, fatigue and physical functioning were experienced differently between men and women. In women compared to men, there was a stronger relationship between physical functioning and apathy; while in men there was a stronger relationship between physical functioning and fatigue, and between fatigue and depression. Overall the SEM model for men accounted for more of the variance in depression scores than for females. Previous research indicated that female gender was a predictor of post-stroke apathy, depression and fatigue. While this was not found in the current study, it does seem that the relationships between these constructs is more complex in women and may be influenced by wider factors which were not accounted for in the model proposed in the current study. Given the stronger relationships between physical functioning and fatigue in men, it can be hypothesised that this gender difference may be linked to expectations within gender roles and that for men the loss of physical functioning plays a greater role in the development of post-stroke fatigue and depression.

Clinical guidelines exist for the assessment of post-stroke depression, and management guidelines are presented in terms of managing depression and physical health conditions. Based on the findings of the current study it can be proposed that the assessment of depression should also include screening for apathy, fatigue and physical functioning. Psychological formulation of post-stroke depression should also include these factors, in order to best provide an idiosyncratic intervention that best suits the needs of the client. This study therefore has a number of clinical implications. By including assessment and measures of apathy, depression and fatigue and their clinical correlates into the clinical psychology assessment, the clinical psychologist can provide a more individualised assessment and formulation of psychological sequelae post-stroke. By having an understanding of the individual client's presentation and co-occurrence of these constructs, the clinical psychologist and other members of the multi-disciplinary team can implement a person-centred intervention which may aim to support the

person in the management of post-stroke psychological factors. For example, activity planning / scheduling may help the person to cope better with fatigue which may in turn impact on their feelings of depression. Similarly, the psychologist may work with the occupational therapist in supporting the person to adapt to changes in physical functioning, such as using aids and appliances, which again may help to support an improvement in mood.

While the results from the current study provide a better understanding of post-stroke apathy, depression and fatigue, and have implications for clinical practice, there are a number of limitations which need to be taken into consideration in interpreting the results. The measurement tools used to assess apathy, depression and fatigue were all validated within stroke populations; however, the extent to which they discriminated between the different disorders was not examined. Discriminant validity has not been reported between the apathy evaluation scale and the geriatric depression scale (GDS), but has been with other depression measures. Three items on the GDS (items 1, 6 and 7) relate to the concept of 'interest', which may be related to apathy and as such these tools may assess overlapping symptomology.

The results of the regression and SEM models need to be interpreted with some caution given that the scores from the Barthel index were not normally distributed and, despite efforts to transform the data, it was not possible to negate the skew in the data. The level of skew within the Barthel scores (S = -1.21, SE = .3), indicated that it was just beyond the acceptable range of skewness between -1 to 1, and as such it was likely that this did not influence the results of the models. It may be that given this negative skew that the sample in the current study was made up of a group of people who are more physically able than the general population of stroke survivors. As such the findings may only relate to people who are largely independent post-stroke, and may not be generalizable to a wider stroke population.

A number of issues arose as a result of using a self-report questionnaire. People with stroke may either under- or over-represent the extent of their difficulties. Having carer-

informed questionnaires may have provided an added level of insight into the difficulties faced by people which may have accounted for biases in self-reporting. The fact that the questionnaires were provided in written form may have excluded people with communication difficulties and may have led to an under-representation of people with right-sided weakness, indicating a left-sided stroke which is more likely to lead to impairments in communication. While looking at the descriptive data it seemed that this study included an adequate representation of people with right-sided weakness, however, it may have been that those people with communication difficulties did not participate in the research.

It is possible that if questionnaires were distributed directly from the research team rather than through staff working in NHS stroke services and voluntary services, that more people would have been identified as meeting the inclusion criteria. Recruitment for the study was low, with a response rate of 16%, which was lower than would have been expected from a postal questionnaire. This low response rate may have been influenced by busy work schedules of the recruiters, who were unable to distribute all of the information packs provided to them. Given that people with stroke often have cognitive difficulties and mood disorders, this may have impacted on their abilities to complete and return the questionnaires. This also may have resulted in a response bias with people with more severe depression not returning the questionnaire, and therefore being under-represented in the current sample. A related difficulty was that people who completed the questionnaires were in receipt of services, either through the NHS or the voluntary sector, and this too may have biased the sample.

Due to the above mentioned difficulties with recruitment, a modest sample size was recruited to the study ($N = 63$), which resulted in the regression models which were proposed apriori not having sufficient power. Based on the descriptive results and correlational analyses, the regression models which were carried out included up to four predictor variables, rather

than the proposed apriori models of having up to 8 predictor variables. As such, the regression models undertaken were sufficiently powered to detect a medium effect size.

There were further limitations in this study. One limitation was the fact that there was no account taken of cognitive functioning and its relationship with apathy, depression and / or fatigue post-stroke. It is well documented that cognitive functioning is associated with post-stroke depression and adding this construct may have led to a more comprehensive understanding of post-stroke depression. Due to cost implications of having to conduct face to face cognitive testing and the large sample size required for this study, it was not possible to include a measure of cognitive functioning in the current study. A further limitation was the wide range of age, with people aged from 55 – 91 years ($\bar{x}$ = 71.8; sd = 9.5 years) recruited into the study. As such, there were both people of working age, and people who were retired at the time of their stroke included in the analyses. This may have impacted on the study results, particularly in thinking about the relationship between physical functioning and apathy, depression and fatigue. People with older age were more likely to have other physical co-morbidities than those of younger age, and by not accounting for age in the regression models, this may have been influenced the results. Similarly, there was a wide variation in the length of time since stroke in the study sample, ranging from one to 364 months ($\bar{x}$ = 53.89; sd = 66.29). Again this may have influenced the results, as it is likely that people who had their stroke a longer time ago would have adapted to changes in their physical abilities. Given the wide variation in time since stroke, any differences between those who were in the more acute phases and those who were longer-time stroke survivors may have been masked by the study sample having this broad range. It may have been helpful to have categorised this variable to look at its relationship with apathy, depression and fatigue post-stroke.

Conclusion

The current study found high rates of apathy (60.3%), depression (58.7%) and fatigue (58.7%) post-stroke. These factors occurred both independently and in unison post-stroke and were all related to poorer physical functioning. A model to account for the inter-relationships between these factors was developed in Structural Equation Modelling. This model accounted for 58% of the variance in depression scores and outlined the roles of apathy, fatigue and physical functioning in post-stroke depression. While this model was significant and a good fit for both men and women, the extent of the relationships between factors was different for men and women and the model did not account for as much variance in depression scores in women. These findings have clinical implications in terms of the assessment, formulation and management of the psychological sequelae of stroke. Clinical assessment of depression post-stroke should adopt a biopsychosocial model where apathy, fatigue, physical functioning and gender are taken into account. This will lead to better ways of understanding an individual's psychological functioning post-stroke and how this is related to physical and social difficulties which may be experienced as a result of stroke. By bearing these factors in mind, more targeted formulation and intervention can be provided to improve the psychological well-being of men and women post-stroke.

References

Agrell, B., & Dehlin, O. (1989). Comparison of six depression rating scales in geriatric stroke patients. *Stroke, 20,* 1190-1194. doi: 10.1161/01.STR.20.9.1190

Andersson, S., Krogstad, J.M., & Finset, A. (1999). Apathy and depressed mood in acquired brain damage: Relationship to lesion localization and psychophysiological reactivity. *Psychological Medicine, 29*(2), 447-456. doi:10.1017/S0033291798008046

Appelros, P. (2006). Prevalence and predictors of pain and fatigue after stroke: A population-based study. *International Journal of Rehabilitation Research, 29*(4), 329-333. doi:10.1097/MRR.0b013e328010c7b8

Asch, D.A., Jedrziewski, K., & Christakis, N.A. (1997). Response Rates to Mail Surveys Published in Medical Journals. *Journal of Clinical Epidemiology, 50*(10), 1129-1136. doi:10.1016/S0895-4356(97)00126-1

British Psychological Society. (2011). *Code of human research ethics.* Leicester: BPS.

Brodaty, H., Liu, Z., Withall, A., & Sachdev, P. S. (2013). The longitudinal course of post-stroke apathy over five years. *The Journal of Neuropsychiatry and Clinical Neurosciences, 25*(4), 283–291. doi:10.1176/appi.neuropsych.12040080

Brodaty, H., Sachdev, P. S., Withall, A., Altendorf, A., Valenzueela, M. J., & Lorentz, L. (2005). Frequency and clinical, neuropsychological and neuroimaging correlates of apathy following stroke – the Sydney Stroke Study. *Psychological Medicine, 35,* 1–10. doi:10.1017/S0033291705006173

Byrne, B.M. (2001). *Structural equation modelling with AMOS: Basic concepts, applications and programming.* London: Lawrence Erlbaum Associates.

Caeiro, L., Ferro, J.M., & Costa, J. (2013). Apathy Secondary to Stroke: A Systematic Review and Meta-Analysis. *Cerebrovascular Diseases, 35*, 23–39. doi:10.1159/000346076

Caeiro, L., Ferro, J.M., & Figueira, M.L. (2012). Apathy in acute stroke patients. *European Journal of Neurology, 19*(2), 291-297. doi:10.1111/j.1468-1331.2011.03508.x

Caeiro, L., Ferro, J. M., Pinho e Melo, T., Canhão P., & Figueira, M.L. (2013). Post-Stroke Apathy: An Exploratory Longitudinal Study. *Cerebrovascular Diseases, 35*(6), 507-513. doi:10.1159/000350202

Carota, A., Berney, A., Aybek, S., Laria, G., Staub, F., GhikaSchmid, F., . . . Bogousslavsky, J. (2005). A prospective study of predictors of poststroke depression. *Neurology, 64*(3), 428-433. doi:10.1212/01.WNL.0000150935.05940.2D

Dam, H. (2001). Depression in stroke patients 7 years following stroke. *Acta Psychiatrica Scandinavica, 103,* 287-293. doi:10.1034/j.1600-0447.2001.103004287.x

Delaney, R.C. & Ravdin, L.D. (1997). The neuropsychology of stroke. In P.D. Nussbaum (Ed.), *Handbook of Neuropsychology and Aging* (315-330). New York: Springer.

Duncan, F., Kutlubaev, M.A., Dennis, M.S., Greig, C., & Mead, G.E. (2012). Fatigue after stroke: A systematic review of associations with impaired physical fitness. *International Journal of Stroke, 7*(2), 157-62. doi:10.1111/j.1747-4949.2011.00741.x

Eaton, W.W., Muntaner, C., Smith, C., Tien, A., & Ybarra, M. (2004). Center for Epidemiologic Studies Depression Scale: Review and revision (CESD and CESD-R). In: M.E. Maruish (Ed.), *The Use of Psychological Testing for Treatment Planning and Outcomes Assessment* (363-377). Mahwah, NJ: Lawrence Erlbaum.

Engel, G.L. (1977). The need for a new medical model: A challenge for biomedicine. *Science, New Series, 196*(4286), 129-136. Retrieved from: http://meagherlab.tamu.edu/M-Meagher/Health%20360/Psyc%20360h%20articles/Engel%201977%20360h.pdf

Glader, E., Stegmayr, B., & Asplund, K. (2002). Poststroke fatigue: A 2-year follow-up study of stroke patients in Sweden. *Stroke, 33,* 1327-1333. doi: 10.1161/01.STR.0000014248.28711.D6

Hackett, M.L., & Anderson, C.S. Auckland Regional Community Stroke (ARCOS) Study Group. (2006). Frequency, management, and predictors of abnormal mood after stroke: The Auckland regional community stroke (ARCOS) study, 2002 to 2003. *Stroke, 37*(8), 2123-2128. doi:10.1161/01.STR.0000231387.58943.1f

Hackett, M.L., Yapa, C., Parag, V., & Anderson, C.S. (2005). Frequency of depression after stroke: A systematic review of observational studies. *Stroke, 36,* 1330-1340. doi: 10.1161/01.STR.0000165928.19135.35

Haghgoo, H.A., Pazuki, E.S., Hosseini, A.S., & Rassafiani, M. (2013). Depression, activities of daily living and quality of life in patients with stroke. *Journal of the Neurological Sciences, 328,* 87-91. doi:10.1016/j.jns.2013.02.027

Hama, S., Yamashita, H., Shigenobu, M., Watanabe, A., Hiramoto, K., Kurisu, K., . . . Kitaoka, T. (2007a). Depression or apathy and functional recovery after stroke. *International Journal of Geriatric Psychiatry, 22*(10), 1046-1051. doi:10.1002/gps.1866

Hama, S., Yamashita, H., Shigenobu, M., Watanabe, A., Kurisu, K., Yamawaki, S., & Kitaoka, T. (2007b). Post-stroke affective of apathetic depression and lesion location: Left frontal lobe and bilateral basal ganglia. *European Archives of Psychiatry and Clinical Neuroscience, 257*(3), 149-152. doi:10.1007/s00406-006-0698-7

Hsueh, I.P., Lin, J-H., & Jeng, J-S., & Hsieh, C-L. (2002). Functional Independence Measure: Comparison of the psychometric characteristics of the functional independence measure, 5 item Barthel index, and 10 item Barthel index in patients with stroke. *Journal of Neurology, Neurosurgery & Psychiatry, 73,* 188–190.

Retrieved from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1737984/pdf/v073p00188.pdf

Intercollegiate Stroke Working Party (2011). *National Sentinel Stroke Clinical Audit 2010 Round 7.* London: Royal College of Physicians.

Intercollegiate Stroke Working Party. (2012). *National Clinical Guidelines for Stroke.* London: Royal College of Physicians.

Krupp, L. B., LaRocca, N. G., Muir-Nash, J., & Steinberg, A. D. (1989). The fatigue severity scale: Application to patients with multiple sclerosis and systemic lupus erythematosus. *Archives of Neurology, 46*(10), 1121-1123. doi:10.1001/archneur.1989.00520460115022

Kutlubaev, M.A., Shenkin, S.D., Farrall, A.J., Duncan, F.H., Lewis, S.J., Greig, C.A., . . . & Mead, G.E. (2013). CT and clinical predictors of fatigue at one month after stroke. *Cerebrovascular Diseases, 3,* 26-34. doi:10.1159/000347113

Lam, S.C., Lee, L.Y.K., & To, K.W. (2010). Depressive symptoms among community-dwelling, post-stroke elders in Hong Kong. *International Nursing Review, 57*(2), 269-273. doi:10.1111/j.1466-7657.2009.00789.x

Lerdal, A., Bakken, L.N., Rasmussen, E.F., Beiermann, C., Ryen, S., Pynten, S., . . . Kim, H.S. (2011). Physical impairment, depressive symptoms and pre-stroke fatigue are related to fatigue in the acute phase after stroke. *Disability and Rehabilitation, 33*(4), 334-342. doi:10.3109/09638288.2010.490867

Mahoney, F. I., & Barthel, D. (1965). Functional evaluation: The Barthel index. *Maryland State Medical Journal, 14,* 56-61.

Marin, R. S., Biedrzycki, R. C., & Firinciogullari, S. (1991). Reliability and validity of the apathy evaluation scale. *Psychiatry Research, 38,* 143-162.

McKevitt, C. Fudge, N., Redfern, J., Sheldenkar, A., Crichton, S., Rudd, . . . Wolfe, C.D.A. (2013). Self-reported long-term needs after stroke. *Stroke, 42,* 1398-1403. doi: 10.1161/STROKEAHA.110.598839

Naess, H., Lunde, L., & Brogger, J. (2012). The triad of pain, fatigue and depression in ischemic stroke patients: The Bergen stroke study. *Cerebrovascular Diseases, 33*(5), 461-465. doi:10.1159/000336760

National Audit Office. (2005). *Reducing Brain Damage: Faster access to better stroke care.* London: The Stationery Office.

National Institute for Health and Clinical Excellence. (2008). *Stroke: Diagnosis and initial management of acute stroke and transient ischemic attack (TIA).* (NICE Clinical Guideline 68). London: National Institute for Health and Clinical Excellence.

National Institute for Health and Clinical Excellence (2009). *Depression in adults with a chronic physical health problem: Treatment and management.* (NICE Clinical Guideline 91). London: National Institute for Health and Clinical Excellence.

National Institute for Health and Clinical Excellence. (2010). *Quality Standard 2 for Stroke.* London: National Institute for Health and Clinical Excellence.

National Institute for Health and Clinical Excellence. (2013). *Stroke rehabilitation: Long-term rehabilitation after stroke* (NICE Clinical Guideline 162). London: National Institute for Health and Care Excellence.

Onoda, K., Kuroda, Y., Yamamoto, Y., Abe, S., Oguro, H., Nagai, A., . . . Yamaguchi, S. (2011). Post-stroke apathy and hypoperfusion in basal ganglia: SPECT study. *Cerebrovascular Diseases, 31*(1), 6-11. doi:10.1159/000319771

Sivrioglu, E. Y., Sivrioglu, K., Ertan, T., Ertan, F.S., Cankurtaran, E., Aki, O., . . . Kirli, S. (2009). Reliability and validity of the Geriatric Depression Scale in detection of

poststroke minor depression. *Journal of Clinical and Experimental Neuropsychology, 31*(8), 999-1006. doi:10.1080/13803390902776878

Snaphaan, L., van der Werf, S., & de Leeuw, F. (2011). Time course and risk factors of post-stroke fatigue: A prospective cohort study. *European Journal of Neurology, 18*(4), 611-617. doi:10.1111/j.1468-1331.2010.03217.x

Tang W.K., Chen Y.K., Liang H.J., Chu, W.C.W., Mok, V.C.T., Ungvari, G.S., & Wong, K.S. (2013). Location of infarcts and apathy in ischemic stroke. *Cerebrovascular Diseases, 35*(6), 566-571. doi:10.1159/000351152

Tang, W.K., Lu, J.Y., Chen, Y.K., Chu, W.C.W., Mok, V., Ungvari, G.S., & Wong, K.S. (2011). Association of frontal subcortical circuits infarcts in poststroke depression: A magnetic resonance imaging study of 591 Chinese patients with ischemic stroke. *Journal of Geriatric Psychiatry and Neurology, 24*(1), 44-49. doi:10.1177/0891988710392375

Taylor-Piliae, R.E., Hepworth, J.T., & Coull, B.M. (2013). Predictors of depressive symptoms among community-dwelling stroke survivors. *Journal of Cardiovascular Nursing, 28*(5), 460-467. doi:10.1097/JCN.0b013e318258ad57

van de Port, I.G.L, Kwakkel, G., Bruin, M., & Lindeman, E. (2007). Determinants of depression in chronic stroke: A prospective cohort study. *Disability and Rehabilitation: An International, Multidisciplinary Journal, 29*(5), 353-358. doi:10.1080/09638280600787047

Whitehead, L. (2009). The measurement of fatigue in chronic illness: A systematic review of unidimensional and multidimensional fatigue measures. *Journal of Pain and Symptom Management, 37*(1), 107-128. doi:10.1016/j.jpainsymman.2007.08.019

Yang, S., Hua, P., Shang, X., Hu, R., Mo, X. & Pan, X. (2013). Predictors of early post ischemic stroke apathy and depression: a cross-sectional study. *BMC Psychiatry, 13,* 164-174. doi:10.1186/1471-244X-13-164

Yesavage, J. A., Brink, T. L., Rose, T. L., Lum, O., Huang, V., Adey, M., & Leirer, V. O. (1983). Development and validation of a geriatric depression screening scale: A preliminary report. *Journal of Psychiatric Research, 17*(1), 37-49. Retrieved from: http://home.uchicago.edu/~/tmurray1/research/articles/at%20least%20read/development%20and%20validation%20of%20a%20geriatric%20depression%20screening%20scale_a%20preliminary%20report.pdf

Zung, W.W. (1965). A self-rating depression scale. *Archives of General Psychiatry, 12,* 63–70. doi:10.1001/archpsyc.1965.01720310065008

Section C:

Appendices of Supporting Material

Cliodhna Carroll

Salomons Centre of Applied Psychology

Canterbury Christ Church University

Appendix A

Data Extraction Form

Article: _____ Author: _____ Database: _____

Year of Publication: ____ Journal: _____

Impact factor: _____ Country of Study: _____

	Participants	**Comparison group**
Age		
Sex		
Time since stroke		
Side of Weakness		
Lesion location		
Community / Acute		
Type of stroke		
n		

Cross-sectional / Longitudinal	Cross ( )	Long ( )
RCT	Yes ( )	No ( )
Intervention study V Observation	Intervention ( )	Observational ( )
Correlation V Regression model	Correlation ( )	Regression ( ) Other ( )
Inclusion / Exclusion criteria described	Yes ( )	No ( )

Outcomes	Outcome	How measured	Notes (include scale limits and reliability/validity of measures and predictors
Depression			
Apathy			
Fatigue			
Other Measures			

Methods
(Was objective stated and appropriate methodology, design and statistical analyses used)

Quality Assessment	
Were non-responders accounted for?	
For intervention / comparison studies, were groups comparable at baseline?	
Were interventions clearly defined?	
Were inclusion / exclusion criteria clearly defined?	
Were the diagnostic tests used appropriate / useful?	
Was the sample representative of the target population?	
Results	
(Briefly state the results from this study)	

Discussion
(Briefly state the discussion from this study & whether it met its objectives; reference to other key papers)

Appendix B

Summary of Articles included in Systematic Literature Review

Authors, Countries & Title	Aims	Sample & Setting	Design & Analysis	Measures	Main findings
*Aben, I., Ladder, J., Honig, A., Lousberg, R., Boreas, A., & Verhey, F.R.J. (2006). Netherlands	Look at the effect of lesion location on development of depression 1 year post-stroke	1 year follow-up study n = 189 Mean age = 68.5 years (sd11.6) Ischemic strokes	SCID / Hamilton depression rating scale Lesion – right v left & anterior v posterior	Depression & lesion location	No significant relationship observed
*Altieri, M., Maestrini, I., Mercurio, A., Troisi, P., Sgarlata, E., Rea, V., . . . Lenzi, G. L. (2012). Italy	Look at predictors of post-stroke depression	30 month follow-up n=105 Mean age = 64.38 (sd11.2) Minor ischemic strokes	BDI – short form DSM-IV clinical interview	Depression & lesion location	No significant relationship observed
*Angelelli, P., Paolucci, S., Bivona, U., Piccardi, L., Ciurli, P., Cantagallo, A., . . . Pizzamiglio, L. (2004). Italy	Look at neuropsychiatric symptoms and its change over time in first year post-stroke	Cross-sectional study n=124 Assessed at 2, 6 & 12 months post-stroke Cerebral ischemic strokes (45 at 2 months, mean age 60.1 [sd12.9]; 45 at 6 months, mean age 62 [sd11.3]; 34 at 12 months, mean age 59.7 [sd11.2])	Neuropsychiatric Interview – informant interview	Depression & gender Apathy & time since stroke	Females more depressed than males (OR=2.67, 95%CI [1, 7.14]) Significant relationship observed – depression greater at 6 & 12 months compared to 2 months, and tended to peak at 6 months (OR=2.65, 95%CI [1.14, 6.05])
Appelros, P. (2006).	Look at pain and fatigue after stroke	n=253	Geriatric depression scale	Depression & fatigue	Depression was significant predictor

		Mean age = 74.5 years Assessed at baseline and at 12 months	Rankin scale NIHSS		of fatigue at 1 year (OR = 3.2, 95%CI [1.7, 6], p < .001)
				Fatigue & physical functioning	Lower physical functioning was significant predictor of fatigue (OR = 1.4, 95%CI [1.2, 1.7, p < .001)
				Fatigue & type of stroke	No significant relationship observed
				Fatigue & stroke severity	Stroke severity was significant predictor of fatigue at 1 year follow-up (OR = 1.11, 95%CI [1, 1.23], p < .05)
*Ayerbe, L., Ayis, S., Rudd, A. G., Heuschmann, P. U., & Wolfe, C. D. (2011). United Kingdom	Look at frequency, predictors and associations of depression 5 years post-stroke	Longitudinal follow-up study n=3689 Measured at 3 months, 1 year, 3 years & 5 years	HADS MMSE Barthel Index	Depression & physical functioning	Low physical functioning related to increased depression (OR ranging from 0.35 – 0.56 at varying timepoints)
				Depression & stroke severity	Significant relationship observed – more severe stroke predicted depression

				Depression & Age Depression & gender	No significant relationship observed No significant difference observed
*Badaru, U.M., Ogwumike, O.O., Adeniyi, A.F., & Olowe, O.O. (2013). Nigeria	Look at ADLs in people with post-stroke fatigue and depression	Cross-sectional study n = 65 Age range: 58 – 80 years	Geriatric depression scale-15 Fatigue severity scale Barthel Index	Depression & physical functioning Fatigue & physical functioning	Significant difference between those with and without depression on physical functioning ($p < .05$) No significant difference between those with and without fatigue on physical functioning
*Berg, A., Palomaki, H., Lehtihalmes, M., Lonnqvist, J., & Kaste, M. (2003). Finland	Look at associates and predictors of depressive symptoms post-stroke	Prospective study over time up to 18 months post-stroke n=100 Mean age = 55.2 (sd10.6) Measured at acute, 2, 6, 12 & 18 months post-stroke	BDI Hamilton Rating Scale for depression DSM-III criteria for depression Barthel index	Depression & lesion location Depression & physical functioning Depression & gender	No significant relationship observed Increased physical functioning related to increased depression ($p < .05$) Conflicting results – at 18 months men had significantly more depression than women ($p < .01$); but no sig difference at acute phase, 2, 6 or

					12 months post-stroke
				Depression & age	Old age related to more depression (r = .27 at acute stage, r = .24 at 2 months and r = .18 at 6 months; p < .05)
				Depression & stroke severity	Sig relationship observed – increased stroke severity associated with increased levels of depression (r = -.3, p < .01 at 6 months)
*Brodaty, H., Liu, Z., Withall, A., & Sachdev, P. S. (2013). Australia	Look at predictors of apathy post-stroke	Longitudinal study over 5 years n = 251 at index; n = 75 at 5 years. Mean age at baseline = 72.1 years(sd 8.85) Measures at baseline (within 1 week of stroke), 3-6 months post-stroke, 1, 3 and 5 years post-stroke.	European stroke severity scale AES GDS-15 item Katz & Akpom ADL scale	Apathy & Depression	Regression: depression was sig predictor of apathy (OR = 1.6, p < .05)
				Apathy & physical functioning	Significant relationship observed – apathetic patients had sig lower ADL scores (lower physical functioning) than non-apathetic patients (OR = -5.1, p < .01).

				Apathy & time since stroke	Significant relationship observed – apathy scores increased significantly over time (OR = 1.8, p < .01)
*Brodaty, H., Sachdev, P. S., Withall, A., Altendorf, A., Valenzueela, M. J., & Lorentz, L. (2005). Australia	To look at clinical, neuropsychological and neuroimaging correlates of post-stroke apathy	Cross-sectional study n=167 Mean age = 72.2 years (sd 8.8) Ischemic stroke	European stroke severity scale AES GDS-15 item Hamilton Rating Scale for Depression Katz & Akpom ADL scale	Apathy & Depression	Significant difference between those with apathy and without on depression scales (more depression in those with apathy) (t = -2.66, p < .01)
				Apathy & physical functioning	Significant difference between apathetic & non-apathetic on physical functioning, apathetic group had poorer physical functioning (t = 3.14, p < .01)
				Apathy & age	Significant relationship – those with apathy were significantly older (t = -2.72, p < .01)
				Apathy & stroke severity	No significant relationship observed

*Brown, C., Hasson, H., Thyselius, V., & Almborg, A.H. (2012). Sweden	Look at factors associated with post-stroke depression	n=181 Mean age = 74 years (range: 32-92 years) Measured at 2 weeks post-discharge following stroke, 3 months & 12 months.	Center of Epidemiologic Studies-Depression Scale Barthel Index	Physical functioning & Depression Depression & gender	Low physical functioning related to increased depression ($r = -.33$, $p < .001$ at 2 weeks; $r = -.26$, $p < .05$ at time 3 months) Conflicting results over time – at 2 weeks post-discharge females were significantly more depressed than males ($t = -2.68(118)$, $p < .01$) but this was not significant at 3 months or 12 months
*Caeiro, L., Ferro, J.M., Santos, C.O., & Figueira, M.L. (2006). Portugal	Look At relationship between post-stroke depression and other factors in acute stroke patients	n=178 Mean age 57 years <= 4 days since stroke 26 subarachnoid haemorrhage 31 intracerebral haemorrhage 121 cerebral infarct	Montgomery Asberg depression rating scale DSM-IV mood disorder due to stroke criteria Gainotti's post stroke depression rating scale	Depression & lesion location	No significant relationship observed
*Caeiro, L., Ferro, J.M., & Figueira, M.L. (2012). Portugal	Look at apathy and relationship to hospitalisation, neuroanatomical factors, depression,	n=94 Mean age = 55.7 years (sd12.9) Acute stroke	AES-10 item Montgomery Asberg depression rating scale	Apathy & Depression	No significant relationship observed in regression

	demographic factors and functional outcome post-stroke	<= 4 days since stroke 22 intracerebral haemorrhage 72 cerebral infarcts	Modified Rankin scale	Apathy & type of stroke	Significant relationship – intracerebral haemorrhage was predictor of apathy (OR=3.5, 95%CI [1.1, 10.8], p < .05)
*Caeiro, L., Ferro, J. M., Pinho e Melo, T., Canhão P., & Figueira, M.L. (2013). Portugal	Look at apathy at 1 year post stroke and relationships with demographic, and clinical factors, depression, cognitive and functional outcome	n=76 Mean age = 62.9 years (SD 10.9)	Apathy Evaluation Scale Montgomery Asberg Depression Rating Scale Barthel Index	Apathy & Depression Apathy & lesion location Apathy & physical functioning	No significant relationship observed in regression No significant relationship observed Significant relationship – apathy associated with worse physical functioning (OR = 2.36, 95%CI [1.24, 4.49], p < .01)
*Carota, A., Berney, A., Aybek, S., Laria, G., Staub, F., GhikaSchmid, F., . . . Bogousslavsky, J. (2005). Switzerland	Look at relationships between early depressive behaviour after stroke and depression at 3 & 12-months post-stroke	Prospective study n=273 Mean age = 64.4 years (sd15.9) Ischemic stroke	DSM-IV Barthel Index	Depression & lesion location Depression & physical functioning Depression & Age	No significant relationship observed Low physical functioning related to increased depression (OR=4.31, 95% CI [2.41, 7.69], p < .05) Younger age (<68 years) significantly related to more

					depression (OR =2.32, 95% CI [1.3, 4.13], $p < .05$)
*Castellanos-Pinedo, F., Maria Hernandez-Perez, J., Zurdo, M., Rodriguez-Funez, B., Maria Hernandez-Bayo, J., Garcia-Fernandez, C., . . . Antonio Castro-Posada, J. (2011). Spain	Look at predictors of psychopathological symptoms post-stroke	Prospective study n=89 Measured at admission, 4, 12 and 26 weeks post-stroke Ischemic stroke	Neuropsychiatric Inventory – Apathy subscale Hamilton Rating Scale for depression Modified Rankin scale Barthel Index	Apathy & lesion location Apathy & physical functioning	No significant relationship observed Apathy was not significantly related to physical functioning as measured by the Barthel index
*Chatterjee, K., Fall, S., & Barer, D. (2010). UK	Look at relationship between physiological, biochemical, neuro-imaging and socio-economic factors and post-stroke depression	Cross-sectional case control study Community based, at least 9 months post-stroke n=127 (40 with depression, 87 without depression) Mean age of depressed was 69 (sd11) and non-depressed was 71 (sd10)	DSM-IV criteria Montgomery-Asberg depression scale Barthel Index	Depression & basal ganglia Depression & Age Depression & physical functioning	Significant relationship observed, those with depression more likely to have lesions in basal ganglia (OR=2.2, $p < .05$) No significant difference between depressed and non-depressed on age No significant difference between depressed and non-depressed on physical functioning

				Depression & time since stroke	No significant difference between depressed and non-depressed on time since stroke
*Chau, J.P.C., Thompson, D.R., Chang, A.M., Woo, J., Twinn, S., Cheung, S.K., & Kwok, T. (2010). China	Look at prevalence and associates of 6-month post-stroke depression	Cross-sectional study n=210 Mean age =71.7 years Ischemic, haemorrhagic and non-specific	Modified Barthel index Geriatric depression scale	Depression & lesion location Depression & physical functioning Depression & type of stroke	No significant relationship observed Low physical functioning related to increased depression (OR=0.97, 95% CI [0.94, 1], p < .05) No significant relationship observed
*Choi-Kwon, S., Han, S.W., Kwon, S.U., & Kim, J.S. (2005). South Korea	Look at factors associated with post-stroke fatigue	Cross-sectional study n=220 Mean age of fatigued was 59.2 years (sd9.2) and of non-fatigued was 61.5 years (sd 8.7) Mean of 15 months post-stroke	Geriatric depression scale Fatigue severity scale Fatigue impact scale Modified Rankin scale	Fatigue & Depression Fatigue & Lesion location Fatigue & physical functioning	Depression was significant predictor of fatigue (OR=2.7, 95%CI [1.04, 6.85], p < .05) No significant relationship with lesion location and fatigue Decreased physical functioning related to increased fatigue

					(OR=3.3, 95%CI [1.29, 8.18], $p < .05$)
				Fatigue & Age	No significant difference between those with and without fatigue on age
*Christensen, D., Johnsen, S.P., Watt, T., Harder, I., Kirkevold, M., & Andersen, G. (2008). Denmark	Look at course of post-stroke fatigue and its clinical features	n=165 Median age was 64.5 years Measured at 10 days, 3months, 1 year and 2 years post-stroke Ischemic & Haemorrhagic strokes	Major depression inventory Multidimensional fatigue inventory Barthel index	Fatigue & physical functioning	Decreased physical functioning related to increased fatigue (β = 2.8, 95%CI [0.9, 4.8])
				Fatigue & time since stroke	No significant relationship observed
*Crosby, G.A., Munshi, S., Karat, A.S., Worthington, E., & Lincoln, N.B. (2012).	Look at frequency of fatigue and impact on daily life	Cross-sectional study n=64 Mean age 73.5 years (sd14)	BASDEC Fatigue severity scale Barthel index	Fatigue & Depression	Significantly higher depression in those with fatigue compared to those without fatigue ($p < .001$)
				Fatigue & physical functioning	No significant relationship observed
				Fatigue & gender	Significant difference –females more depressed than males ($p < .001$)

				Fatigue & age Fatigue & time since stroke Fatigue & type of stroke	No significant relationship observed No significant relationship observed No significant relationship observed
*Dam, H. (2001). Denmark	Look at frequency and correlates of depression 7 years post-stroke	Cross-sectional study n=99 Mean age = 57 (sd8.5) 7 years post-stroke	BDI Hamilton depression rating scale ADLs	Depression & lesion location Depression & physical functioning Depression & gender Depression & previous Mental health	No significant relationship observed No significant relationship observed Females more depressed than males ($p < .05$) No significant relationship observed
*Effat, S.M., Mohamed, M.M., El Essawy, H.I., El Sheikh, M.M., & Abdul Aal, H.S. (2011). Egypt	Look at predictors of post-stroke depression	n=120 Mean age of post-stroke depression group was 54.96 (sd4.8) Mean age of non-depressed group was 58.43 (sd4.4)	Mini International Neuropsychiatric Interview Hamilton rating scale for depression Barthel Index	Depression & lesion location	Significant relationship to frontal region - depressed group had a statistically significant frontal lesion compared to the non-depressed patients ($\chi^2 = 5.07$, $p < .05$)

				Depression & physical functioning	Low physical functioning related to increased depression ($\chi^2 = 23.83$, $p < .001$ on moderate dependency on BI)
				Depression & gender	Males more depressed than females ($\chi^2 = 13.39$, $p < .001$)
				Depression & Age	Younger age significantly related to more depression ($p < .05$)
*Feigin, V.L., Barker-Collo, S., Parag, V., Hackett, M.L., Kerse, N., Barber, P.A., . . . Auckland Regional Community Stroke Study Group. (2012). New Zealand	Look at predictors of post-stroke fatigue in a community sample	n=613 Mean age 69.9 years (sd:13) 6 months post-stroke Ischemic stroke	GHQ-28 – depression subscore Short form 36 vitality score (energy & fatigue) Barthel Index	Fatigue & Depression	Depression was significant predictor of fatigue (OR = 12.42, 95%CI [5.94, 25.94]) Fatigued were more depressed than non-fatigued ($p < .001$)
				Fatigue & physical functioning	Decreased physical functioning related to increased fatigue ($p < .001$)

				Fatigue & age Fatigue & gender	Older age significantly related to more fatigue ($r = -.12$, $p < .01$) No significant difference between men & women on fatigue
*Fuller-Thomson, E., Tulipano, M.J., & Song, M. (2012). Canada	Look at frequency and correlates of post-stroke depression	Cross-sectional study n=858 Mean age = 63.8 years (sd16.3) Included mild CVA	CIDI-Short Form	Depression & age	Younger age sig related to more depression (OR for those younger than 65 ranged from 7.1 in those < 30years to 2.76 for those aged 50-64 years, compared to those > 65 years).
*Gainotti, G., Azzoni, A., & Marra, C. (1999). Italy	Look at whether post-stroke depression is linked to organic or to psychosocial factors	Cross-sectional study n=153 Mean age was 61.9 at < 2 months, 63.4 at 2-4 months and 61.5 years at > 4 months Assessed some people at < 2months, some at 2-4 months and more at > 4 months post-stroke		Depression & time since stroke Depression & lesion location	Significant relationship – depression increases over time ($\chi^2 = .004$) No significant relationship observed
*Greenop, K.R., Almeida, O.P.,	Look at the relationship between	Prospective study n=61	Hospital Anxiety and Depression Scale	Depression & age	No significant relationship observed

Hankey, G. J., van Bockxmeer, F., & Lautenschlager, N.T. (2009). Australia	premorbid personality and post-stroke behavioural and psychological symptoms	Mean age = 65.69 years (sd10.96) Follow-up 3 months post-stroke			between NPI depression score and age
*Hackett, M.L., & Anderson, C.S. Auckland Regional Community Stroke (ARCOS) Study Group. (2006). Australia	Look at predictors of post-stroke depression	Community, prospective study n=739 Mean age = 69.2 years(sd13.4)	GHQ-28 Barthel Index	Depression & physical functioning	Low physical functioning related to increased depression (OR = 2.35, 95% CI [1.33, 4.14])
				Depression & gender	No significant difference observed
				Depression & previous Mental health	Significant positive relationship (OR = 2.14, 95% CI [1.34, 3.43])
				Depression & age	No significant relationship observed
				Depression & type of stroke	No significant relationship observed
*Haghgoo, H.A., Pazuki, E.S., Hosseini, A.S., & Rassafiani, M. (2013). Iran	Look at relationship between activities of daily living and post-stroke depression	n=40 Mean age = 61.5 years (sd3.5) Mean of 8.7 months post-stroke	BDI-II Modified Barthel index	Depression & physical functioning	Low physical functioning related to increased depression ($r = -.82$, $p < .001$)
				Depression & gender	

					Females more depressed than males ($p < .05$).
*Hama, S., Yamashita, H., Shigenobu, M., Watanabe, A., Kurisu, K., Yamawaki, S., & Kitaoka, T. (2007b). Japan	Look at relationship between damage to basal ganglia & post-stroke depression	Cross-sectional study n=243 Mean age = 65.2 years (sd11.3) Haemorrhagic / occlusive stroke	Japanese version of Zung Self-rating depression scale Japanese version of Apathy Scale	Depression & lesion location Apathy & basal ganglia	Significant relationship to left frontal region ($p < .05$), but not to damage in the basal ganglia Significant relationship with basal ganglia damage in right and left hemispheres ($p < .05$), but not significantly related to frontal lobe damage.
*Hilari, K., Northcott, S., Roy, P., Marshall, J., Wiggins, R.D., Chataway, J., & Ames, D. (2010). UK	Look at factors that predicted psychological distress in the first six months post-stroke	Prospective longitudinal study n=87 (including 32 with aphasia) Mean age = 69.7(sd14.1) Measured at baseline, 3 months and 6 months	GHQ-12 Barthel index NIHSS	Depression & physical functioning Depression & age	Low physical functioning related to increased depression – at 3 months ($r = -.27$, $p < .05$) & 6 months post-stroke ($r = -.32$, $p < .01$) At baseline, younger age was associated with depression ($r = -.24$, $p < .05$), but not a sig predictor in

					regression. No significant relationship between age and distress at 3 & 6 months.
				Depression & stroke severity	Significant relationship observed – more depression related to more severity at baseline ($r = .3$, $p < .05$), at 3 months ($r = .28$, $p < .05$) and at 6 months ($r = .28$, $p < .05$). In regression, stroke severity was significant predictor of psychological distress at baseline (Wald's $\chi 2 = 7.95$, $p < .01$), but not at 3 & 6 months.
*Hsieh, L. P., & Kao, H.J. (2005). Taiwan	Look at prevalence of depressive symptoms and clinical correlates	n=207 Mean age = 64 years Ischemic strokes	Hamilton depression Rating scale Barthel Index Modified Rankin scale	Fatigue & Lesion location Depression & physical functioning	No significant relationship observed Low physical functioning related to increased depression ($r = -.38$; $p < .001$)

				Depression & gender	Females more depressed than males ($p < .01$)
				Depression & age	No significant relationship observed
				Depression & time since stroke	No significant relationship observed
*Hubacher, M., Calabrese, P., Bassetti, C., Carota, A., Stocklin, M., & Penner, I. (2012). Switzerland & Germany	Look at fatigue after acute stage of stroke	n=31 Mean age = 59.29 years (sd10.3) Mean of 50.65 days post-stroke (sd31.57 days). Measured at baseline and after 4 weeks	BDI Fatigue severity scale Modified fatigue impact scale	Depression & fatigue	Significant correlation ($r = .46$, $p < .01$)
				Fatigue & time since stroke	No significant relationship observed
*Ingles, J., Eskes, G., & Phillips, S. (1999). Canada	Look at frequency of post-stroke fatigue and impact on depression and functioning	Community based n=88 Mean age = 66.6 years (sd13.4) Measured 3-13 months post-stroke	Fatigue impact scale Geriatric depression scale	Fatigue & depression	Depression was significant predictor of fatigue ($\beta = .27$, $p < .05$)
				Fatigue & Lesion location	No significant relationship observed
				Fatigue & physical functioning	No significant relationship observed
				Fatigue & Gender	No significant difference observed

				Fatigue & age Fatigue & time since stroke Fatigue & stroke severity Depression & gender Depression & age	No significant relationship observed No significant relationship observed No significant relationship observed No significant relationship observed No significant relationship observed
*Kaji, Y., Hirata, K., & Ebata, A. (2006). Japan	Look at prevalence and clinical correlates of post-stroke depression	n=100 Mean age = 64.6 years (sd11.6) Measured 2-5 weeks since stroke	DSM-IV criteria Zung rating scale for depression Mini-Neuropsychiatric Inventory Hamilton Depression scale Apathy evaluation scale	Depression & lesion location Apathy & gender Depression & gender Depression & age	No significant relationship observed Female gender was significant predictor of apathy ($p < .05$) No significant difference observed No significant relationship observed
*King, R.B., Shade-Zeldow, Y., Carlson, C.E., Feldman, J.L., & Philip, M. (2002).	Look at adaptation to stroke and identify predictors of depressive symptoms	Longitudinal study n=53 Mean age = 61 years (*SD* = 11.9)	CES-D	Depression & social support	Significant relationship ($\beta = -.28$, $p < .05$)

US		Measured at 4 time points – pre-discharge, 6-10 weeks post-discharge, 1 years and 2 years post-discharge		Depression & time since stroke	Depression decreases significantly over time ($F(3,50) = 2.88$, $p < .05$). A significant decrease only between pre-discharge and 2 years post-stroke ($t(52) = 2.8$, $p < .01$)
*Kouwenhoven, S.E., Gay, C.L., Bakken, L.N., Lerdal, A. (2013). Norway	to estimate the prevalence of post-stroke depression (PSD) in the acute phase following first-ever stroke, and to identify its sociodemographic and clinical correlates	Cross-sectional study n=109 Mean age 68.3 years(sd13.1) Measured within 15 days of hospitalisation	BDI-II Fatigue severity scale Barthel index	Depression & lesion location Depression & Fatigue Depression & age Depression & stroke type Depression & gender Depression & physical functioning	No significant relationship observed Significant positive correlation ($p < .001$) No significant relationship observed No significant relationship observed No significant relationship observed No significant relationship observed
*Ku, H., Chen, C., Yang, Y., Hu, C., Wu, D., Chen, C., Chen, P., & Chi, N. (2013).	Look at relationship between stroke location and depression and anxiety post-stroke	Prospective study n=26 Mean age = 60.8 years (sd8.7)	Hospital anxiety and depression scale MINI NIHSS Barthel index	Depression & physical functioning	Low physical functioning related to increased depression ($p < .05$ at 1 week

Taiwan		Measured at 1 week and 1 month post-stroke			and 1 month post-stroke)
				Depression & stroke severity	No significant relationship observed
				Depression & age	No significant relationship observed
*Kutlubaev, M.A., Shenkin, S.D., Farrall, A.J., Duncan, F.H., Lewis, S.J., Greig, C.A., Dennis, M.S., Wardlaw, J.M., MacLullich, A.M.J., & Mead, G.E. (2013).	Look at relationships between neuroanatomical factors and post-stroke fatigue at 1 month post-stroke	n=107 Mean age = 70.5 1 month post-stroke Ischemic / haemorrhagic stroke	Hospital Anxiety and Depression Scale Fatigue assessment scale	Depression & Fatigue	Depression was significant predictor of fatigue ($\beta = 0.30$, $p < .01$)
				Fatigue & Lesion location	Significantly more fatigue in those with posterior circulation strokes compared to other strokes ($KW = 6.2$, $p < .05$)
				Fatigue & gender	Women had higher FAS scores [median = 25; interquartile range (IQR) = 19–33] than men (median = 22.6; IQR = 18–28.25) ($U = 1062$, $p < .05$).
				Fatigue & stroke severity	No significant relationship observed

				Fatigue & Age	No significant relationship observed
*Lam, S.C., Lee, L.Y.K., & To, K.W. (2010). China	Look at prevalence of post-stroke depressive symptoms and their clinical and demographic correlates	Community dwelling Cross-sectional study n=50 Mean age = 75.42	GDS-15 item Simplified Barthel index	Depression & physical functioning	Low physical functioning related to increased depression ($r = -.48$, $p < .001$)
				Depression & social support	Significant relationship – lower social support related to more depressive symptoms ($r = -.29$, $p < .05$)
				Depression & type of stroke	No significant relationship observed
*Lerdal, A., Bakken, L.N., Rasmussen, E.F., Beiermann, C., Ryen, S., Pynten, S., . . . Kim, H.S. (2011). Norway	Look at prevalence and demographic and clinical correlates of post-stroke fatigue	Cross-sectional study in first 2 week post-stroke n=115 Mean age = 68.3 years(sd13.2)	BDI Fatigue severity scale	Fatigue & Depression	Depression was significant predictor of fatigue ($\beta = .31$, $p < .05$)
				Fatigue & physical functioning	Decreased physical functioning related to increased fatigue ($r = -.19$, $p < .05$)
				Fatigue & gender	No significant difference observed
*Lerdal, A., & Gay, C.L. (2013). Norway	To determine whether fatigue in the acute phase following	n=96 Mean age = 67.8 years (sd12.9)	Fatigue Severity Scale Beck Depression Inventory II	Fatigue & time since stroke	No significant difference in fatigue scores over time

	stroke predicts long-term patient-reported physical and mental health outcomes 18 months later	Assessed within 2weeks of first-ever stroke and 18 months later		Fatigue & depression Fatigue & Age Fatigue & gender	Fatigue & depression significantly related at 2 weeks ($r = .465$, $p < .05$) and at 18 months post-stroke ($r = .21$, $p < .05$) No significant relationship observed No significant difference observed
*Li, S.C., Wang, K.Y., & Lin, J.C. (2003). Taipei	Look at post-stroke depression and related factors	Cross-sectional study n=106 Mean age = 71.9 years Time since stroke ranged from 0.5 months-120 months	GDS-30 Barthel index	Depression & Physical functioning Depression & gender Depression & social support Depression & age	No significant relationship observed No significant relationship observed Significant relationship – negatively correlated ($r = -.31$, $p < .01$) No significant relationship observed
*Ligthart, S.A., Richard, E., Fransen, N.L., Eurelings, L.S.M., Beem, L., Eikelenboom, P., . . . Moll van Charante, E.P.	To assess the relationship between symptoms of apathy and cardiovascular risk factors or disease	Cross-sectional Community setting n=3534; 346 with stroke Median age 74.3 years (range: 70-78 years)	GDS-15 item 3 items from GDS used to measure apathy	Depression & Apathy	There were people with apathy without depression

(2012). Netherlands	(stroke or other) in people without depression or dementia.				
*Lincoln, N.B., Brinkmann, N., Cunningham, S., Dejaeger, E., De Weerdt, W., Jenni, W., … De Wit, L. (2013). European study – UK, Germany, Belgium, Switzerland	Look at prevalence and predictors of post-stroke depression and anxiety in 4 European centres	n=220 Assessed at 2, 4 & 6 months & 5 years post-stroke	Hospital Anxiety and depression scale NIHSS Barthel index Nottingham extended Activities of Daily living	Depression & physical functioning Depression & gender Depression & age Depression & stroke severity	No significant relationship observed No significant difference observed Old age related to more depression (β = .23, $p < .001$) No significant relationship observed
*MacHale, S.M., O'Rourke, S.J., Wardlaw, J.M., & Dennis, M.S. (1998). UK	Look at relations between lesion location and post-stroke psychiatric illness	n=55 Mean age = 66 years	Hospital anxiety and depression scale Barthel index DSM-IV criteria for depression	Depression & lesion location Depression & physical functioning	Those with right hemispheric lesions more likely than left to be depressed (OR = 6, 95%CI [1.4, 25.2], $p < .05$) and those with right anterior lesions more likely to be depressed than any other group (OR = 11,95% CI [2.5, 49.7], $p < .05$) Those with lower physical functioning significantly more

				Depression & age	likely to be depression (U=954, p < .01) Younger people significantly more likely to be depression (U=1201, p < .05)
*Marin, R.S., Firinciogullari, S., & Biedrzycki, R.C. (1994). US	Look at discriminability of apathy and depression by looking at differences between diagnostic groups	n=123; left hemisphere stroke n = 18; right hemisphere stroke n = 22. Mean age = 72 years	Hamilton rating scale for depression Apathy evaluation scale	Apathy & Depression	Apathy and depression significantly correlated (r = .49, p < .05) in people with left hemisphere stroke No significant correlation between apathy and depression in people with right hemisphere stroke
*Mead, G., Graham, C., Dorman, P., Bruins Slot, K., Lewis, S.C., Dennis, M.S. & Sandercock, P.A.G. (2011). UK	Look at associates of post-stroke fatigue	n=1020 Mean age = 71.1 years (sd 10.8) Mean of 64 weeks post-stroke	SF-36	Fatigue & gender Fatigue & age	Significant predictor (females have greater fatigue than males) Older age significant predictor of more fatigue

*Mikami, K., Jorge, R.E., Moser, D.J., Jang, M., & Robinson, R.G. (2013). USA	Look at differences between those with and without post-stroke apathy on cognitive physical and social functioning	Prospective study n=55 (23 with apathy, 33 without apathy) Measured at initial, 3, 6, 9 and 12 months post-stroke	Functional Independence Measure	Apathy & physical functioning	Significant relationship observed
*Murakami, T., Hama, S., Yamashita, H., Onoda, K., Kobayashi, M., Kanazawa, J., Yamawaki, S., & Kurisu, K. (2013). Japan	Look at areas where lesions occur associated with post-stroke depression and other correlates	Cross-sectional study n=149 Mean age = 66.8 years (sd10.3)	Hospital Anxiety and Depression Scale Apathy Scale	Apathy & lesion location Depression & basal ganglia	Significant relationship between apathy and brainstem region Significant relationship observed
*Naess, H., Lunde, L., & Brogger, J. (2012b). Norway	Look at clusters of post-stroke symptoms (pain, depression and fatigue)	Cross-sectional study n=328 Mean age = 67.7 years	Hamilton depression rating scale Fatigue severity scale Rankin scale Barthel Index NIHSS	Fatigue & depression Depression, fatigue & physical functioning Fatigue, depression & previous Mental health	Depression was significant predictor of fatigue ($r = .49$, $p < .001$) Low physical functioning related to increased depression and fatigue ($r = -.33$, $p < .001$) Significant relationship – previous mental health associated

					with more than one post-stroke symptom
*Naess, H., Lunde, L., Brogger, J., & Waje-Andreassen, U. (2012a). Norway	Look at characteristics and mortality related to post-stroke fatigue	n=377 Postal questionnaire 6 months post-stroke	Fatigue severity scale Hospital anxiety and depression scale Barthel index	Fatigue & Depression	Depression was significant predictor of fatigue (OR = 4.1, $p < .05$)
				Fatigue & basal ganglia	No significant relationship observed
				Fatigue & gender	Significant difference between fatigued and non-fatigued on gender ($p < .01$) with females more likely to be fatigued
				Fatigue & age	Older age significantly related to more fatigue ($p < .05$)
				Fatigue & physical functioning	Those with fatigue are more likely to have poorer physical functioning than those without fatigue ($p < .001$)
*Naess, H., Nyland, H. I., Thomassen, L., Aarseth, J., & Myhr, K. (2005).	Look at impact of ischemic stroke in young people	n=192 Mean age = 47.8 Mean 6 years post-stroke	MADRS Fatigue severity scale Rankin scale	Fatigue & depression	Depression was sig predictor of fatigue ($p < .001$)

Norway				Fatigue & physical functioning	Decreased physical functioning related to increased fatigue ($p < .001$)
				Fatigue & Gender	No significant difference observed
				Fatigue & Age	No significant relationship observed
*Nys, G.M.S., van Zandvoort, M.J.E., van der Worp, H.B., de Haan, E.H.F., de Kort, P.L.M., & Kappell, L.J. (2005). Netherlands	Look at relations between post-stroke depressive symptoms and cognition and lesion characteristics	n=126 Mean age 62.3 years (sd13.3) Assessed 3 weeks post-stroke	Montgomery Asberg depression rating scale Modified Barthel index Rankin scale	Depression & lesion location	No significant relationship observed
				Depression & physical functioning	Low physical functioning related to increased depression ($p < .01$)
				Depression & gender	No significant difference observed
				Depression & age	No significant relationship observed
*Okada, K., Kobayashi, S., Yamagata, S., Takahashi, K., & Yamaguchi, S. (1997). Japan	Look at severity of apathy and relationship to regional cerebral blood flow	n=40 Mean age = 71.4 years Mean of 16.2 months post-stroke	Zung rating scale of depression Apathy scale Rankin scale	Looked at difference between apathy and depressed groups	Apathetic group had higher depression than non-apathetic group
				Apathy & lesion location	No significant relationship observed

				Apathy & Cerebral blood flow	Significant relationship observed – apathetic group had reduced rCRF in right dorsolateral frontal and left frontotemporal regions compared to non-apathetic group
*Onoda, K., Kuroda, Y., Yamamoto, Y., Abe, S., Oguro, H., Nagai, A., . . . Yamaguchi, S. (2011). Japan	Look at rCBF in apathetic and non-apathetic patients after stroke.	n=102 Assessed within 1 month of stroke	Self-rating depression scale Apathy scale	Looked at difference between apathy and depressed groups	Apathetic group had higher depression than non-apathetic group ($p < .001$)
				Apathy & basal ganglia	Left basal ganglia lesions were significantly associated with apathy ($\chi 2 = 7.51$, $p < .01$)
				Apathy & physical functioning	No significant relationship observed
				Apathy & gender	No significant difference observed
				Apathy & age	No significant relationship observed
*Paradiso, S., & Robinson, R.G. (1999).	Look at difference between major and	n=141 Mean age of those with minor	DSM-IV criteria for major & minor depression	Depression & lesion location	More major than minor depression in those with left

	minor depression after stroke.	depression = 56.8 years Mean age of those with major depression = 52.1 years			hemisphere lesions ($p < .005$) More major than minor depression in those with anterior lesions ($p < .05$)
				Depression & Age	Younger age had more major than minor depression ($p < .05$)
*Park, J.Y., Chun, M.H., Kang, S.H., Lee, J.A., Kim, B.R., & Shin, M.J. (2009). Korea	Look at influence of post-stroke fatigue on functional outcome	n=40 Mean of 32.7 months post-stroke	BDI Fatigue severity scale Barthel Index	Depression & fatigue	Significant correlation ($r = .47$, $p < .05$)
				Fatigued compared to non-fatigued, looking at depression	No significant difference between fatigued and non-fatigued groups on depression
				Fatigue & physical functioning	No significant relationship observed
*Quaranta, D., Marra, C., & Gainotti, G. (2012). Italy	Look at psychopathological factors associated with post-stroke depression	n=98 Mean age = 63 years (sd11.2) Within 6 months of stroke Ischemic stroke	Post-stroke depression rating scale – depression measured as subscale depressive and anxiety symptoms Barthel index	Apathy & Lesion location	Left anterior region was significant predictor of apathy ($\beta = .55$, $p < .05$)
				Depression & physical functioning	Low physical functioning predictor of depression ($\beta = -.07$, $p < .001$)

			Apathy – subscale of PSDRS called Reduced Motivation	Depression & gender	Females more depressed than males ($t = 2.839$, $p < .01$)
				Depression & previous Mental health	Previous mood disorder significant predictor of depression ($\beta = .55$, $p < .01$)
				Apathy & age	Higher age significant predictor of apathy ($\beta = .02$, $p < .05$)
*Radman, N., Staub, F., AboulafiaBrakha, T., Berney, A., Bogousslavsky, J., & Annoni, J. (2012). Switzerland	Look at relationships and predictors of post-stroke fatigue	Prospective study n=99 Mean age = 50.9 years (sd14.1) Assessed at acute stage, 6 months and 12 months post-stroke	Hamilton depression rating scale DSM-IV major depression criteria Fatigue Assessment inventory Modified Rankin scale NIHSS	Fatigue & Depression	Depression was significant predictor of fatigue (OR = 1.33, 95%CI [1.14, 1.55], $p < .001$)
				Fatigue & Lesion location	No significant relationship observed
*Raju, R. S., Sarma, P. S., & Pandian, J.D. (2010). India	Look at psychological outcomes and functional independence post-stroke and the relationship with stroke characteristics	n=162 Mean age = 54.3 years (sd12.9) Mean time since stroke = 18.3 months	Hospital anxiety and depression scale Functional Independence measure NIHSS	Depression & physical functioning	Low physical functioning related to increased depression ($r = -.47$, $p < .001$) Physical functioning significant predictor of depression (OR =

					4.4, 95% CI [1.80, 10.76], $p < .01$)
				Depression & age	No significant relationship observed
				Depression & stroke severity	Depression significantly positively correlated with stroke severity ($r = .27$, $p < .01$)
*Rush, B.K., McNeil, R.B., Gamble, D.M., Luke, S.H., Richie, A.N., Albers, C.S., . . . Meschia, J.F. (2010). US	Look at behavioural symptoms post-stroke and their clinical characteristics	n=53 Mean age = 70 years (sd12) Mean time since stroke = 28 months Ischemic stroke	BDI Barthel index Neuropsychiatric inventory	Depression & lesion location	No significant relationship observed
*Santa, N., Sugimori, H., Kusuda, K., Yamashita, Y., Ibayashi, S., & Lida, M. (2008). Japan	Look at frequency of apathy post-stroke and to prospectively study the impact of apathy on functional recovery	Prospective study n=67 Age: 45-90 years	Zung self-rating depression scale Apathy scale Barthel index NIHSS	Apathy & Depression	No significant difference between those with and without apathy on depression scores
				Apathy & age	Apathetic group were significantly older than non-apathetic group ($p < .05$)
				Apathy & stroke severity	No significant difference between

					apathetic and non-apathetic groups observed
				Apathy & Gender	No significant difference observed
				Apathy & physical functioning	No significant difference observed
*Schepers, V., Post, M., Visser-Meily, A., van de Port, I., Akhmouch, M., & Lindeman, E. (2009). The Netherlands	Look at 3-year post-stroke depressive symptoms and the predictors of same	n=131 Mean age = 56.3(sd10.7) Assessed 6 months, 1 year and 3 years post-stroke	Center of Epidemiologic Studies Depression (CES-D) scale Fatigue severity scale Barthel index	Depression and fatigue	No significant relationship observed
				Depression & gender	Female gender significant predictor of post-stroke depression at 3 years (OR = 0.17, 95% CI [0.04, 0.78], $p < .05$)
				Depression & age	No significant relationship observed
				Type of stroke	No significant relationship observed
				Depression & physical functioning	No significant relationship observed
				Depression & time since stroke	Significant decline in depression scores from 1 year to 3

					years post-stroke ($p < .01$)
*Schepers, V., Visser-Meily, A.M., Ketelaar, M., & Lindeman, E. (2006). The Netherlands	Look at fatigue during the first year post-stroke and look at relations between fatigue and personal characteristics, stroke characteristics	n=167 Mean age = 56.4 (sd11.4) Assessed at admission, 6 & 12 months post-stroke	Center of Epidemiologic Studies Depression (CES-D) scale Fatigue severity scale	Depression & fatigue Fatigue & time since stroke Fatigue & age	Depression was significant predictor of fatigue ($\beta = .34$, $p < .001$) There was a significant effect of time, with fatigue increasing over time ($F(2,165) = 10.95$, $p < .001$). Older age significant predictor of fatigue ($\beta = .17$, $p < .05$)
*Sienkiewicz-Jarosz, H., Milewska, D., Bochynska, A., Chelmniak, A., Dworek, N., Kasprzyk, K., . . . Ryglewicz, D. (2010). Poland	Look at associations between demographic, socioeconomic and clinical factors and post-stroke depressive symptoms	Prospective cohort study n=242 Mean age in depressed group = 66.1 (sd12) and in non-depressed group = 65.2 (sd13.7)	GDS-15 item Barthel index Modified Rankins scale NIHSS	Depression & physical functioning Depression & stroke severity	Low physical functioning significant predictor of depression (OR =4.6, 95%CI [1.9, 10.8], $p < .001$) Those with depression compared to those without have higher levels of stroke severity at 3 months post-stroke ($p < .01$)

*Snaphaan, L., van der Werf, S., & de Leeuw, F. (2011). The Netherlands	Look at pre-stroke factors and relationship to post-stroke fatigue	n=108 Mean age = 65 years Assessed 2 and 18 months post-stroke	Hospital anxiety and depression scale NIHSS Barthel index	Fatigue & depression	Depression was significant predictor of post-stroke fatigue (OR = 1.4, 95%CI [1.21, 1.63])
				Fatigue & Lesion location	Infratentorial region infarcts were significant predictors of post-stroke fatigue (OR = 4.69, 95%CI [1.03, 21.47])
				Fatigue & age	Older age significantly related to less fatigue (OR = 0.95, 95% CI [0.91, 0.98])
				Fatigue & physical functioning	No significant relationship observed at 18 months
				Fatigue & Lesion location	No significant relationship observed
*Starkstein, S.E., Fedoroff, J.P., Price, T.R., Leiguarda, R., & Robinson, R.G. (1993). US	Look at frequency and correlates of post-stroke apathy	Prospective study n=80 Assessed < 10 days post-stroke	Present state exam DSM-III depression criteria Hamilton rating scale for depression Apathy scale - abridged	Looked at difference between apathy and depressed groups	No significant difference observed on apathy between depressed and non-depressed groups

				Apathy & Lesion location	Apathy was significantly related to lesions in the posterior limb capsule ($\chi^2 = 7.81$, df = 3, $p < .05$)
				Apathy & age	Apathy significantly related to older age ($F(1,76) = 3.96$, $p < .05$)
*Tang W.K., Chen Y.K., Liang H.J., Chu, W.C.W., Mok, V.C.T., Ungvari, G.S., & Wong K.S. (2013a). China	Look at associations between post-stroke apathy and the location of infarcts	n=185 Mean age = 65.2 (sd10.2)	GDS-15 item Apathy evaluation scale NIHSS Barthel index	Apathy & Depression	Apathetic group had higher depression than non-apathetic group ($p < .001$) Depression was sig predictor of post-stroke apathy (OR = 1.1, 95%CI [1.3, 1.8])
				Apathy & lesion location	Acute pontine infarcts significant predictor of post-stroke apathy (OR = 3.8, 95%CI [1.1, 12.9])
				Apathy & physical functioning	Apathetic group had lower physical functioning than non-

					apathetic group ($p < .001$)
				Apathy & stroke severity	Apathetic group had higher levels of stroke severity than non-apathetic ($p < .01$)
				Apathy & age	Higher age was significant predictor of apathy (OR = 1.1, 95%CI [1, 1.2])
*Tang, W.K., Liang, H.J., Chen, Y.K., Chu, W.C.W., Abrigo, J., Mok, V.C.T., . . . Wong, K.S. (2013b). China	Look at relationship between caudate nucleus and post-stroke fatigue	n=500 Mean age = 65.2 years (sd10.7) 3 months post-stroke	GDS Fatigue severity scale Barthel index NIHSS	Fatigue & physical functioning	Fatigued group have lower physical functioning than non-fatigued ($p < .05$)
				Fatigue & gender	Fatigued group more likely to be women ($p < .01$)
				Fatigue & age	No significant difference between fatigued and non-fatigued on age
				Fatigue & stroke severity	No significant difference between fatigued and non on severity

				Fatigue & depression	Fatigued have significantly higher depression than non-fatigued ($p < .001$)
				Fatigue & Lesion location	Fatigued have more lesions in caudate than non-fatigued ($p < .01$)
*Tang, W.K., Lu, J.Y., Chen, Y.K., Chu, W.C.W., Mok, V., Ungvari, G.S., & Wong, K.S. (2011). China	Look at MRI correlates of post-stroke depression	n=591 Mean age = 66 years (sd11.8) Assessed 3 months post-stroke	DSM-IV depression criteria	Depression & lesion location	Infarcts in frontal region were significantly associated with post-stroke depression ($p < .05$)
				Depression & gender	Females more depressed than males ($p < .01$) Female gender significant predictor of depression (OR = 2.78, 95%CI [1.53, 5.05], $p < .01$)
				Depression & previous MH	Those with previous depression more likely to be in depressed than non-depressed group ($p < .001$)

				Depression & stroke severity	Previous Mental health significant predictor of depression (OR = 9.89, 95%CI [2.69, 36.41], p < .01) Those with more stroke severity more likely to be in depressed group (p < .05)
*Taylor-Piliae, R.E., Hepworth, J.T., & Coull, B.M. (2013). USA	Look at predictors of depressive symptoms in chronic stroke	n=100 Mean age = 70 years (sd10) Mean time since stroke = 39 months (sd49)	CES-D SF-36 Modified Rankin scale Multidimensional scale of perceived social support	Depression & previous Mental health Depression & social support Depression & age Depression & time since stroke Depression & gender	Significant relationship (r = .46, p < .01) Significant relationship - those with less social support have higher depression scores (β = -1.53, p < .05) No significant relationship observed No significant relationship observed No significant relationship observed

				Depression & physical functioning	No significant relationship observed
*Thompson, S.C., SobolewShubin, A., Graham, M.A., & Janigian, A.S. (1989). USA	Look at the severity of stroke and patients' cognitive adaptation to their situation, the relationship with the caregiver, caregivers' adaptation and patient depression and motivation in outpatient therapy.	Cross-sectional study n=40 Mean age = 62.9 years Mean of 9 months post-stroke	Geriatric depression scale	Depression & time since stroke	Significant relationship – depression increases over time ($r = .4$, $p < .01$)
*Townend, E., Tinson, D., Kwan, J., & Sharpe, M. (2010). UK	Look at association between acceptance of disability with post-stroke depression and its ability to predict depression at follow-up	n=89, & 81 at follow-up Mean age = 70.13(sd11.29) Assessed 1 month post-stroke and 9 months post-stroke	SCID Barthel index NIHSS	Depression & physical functioning	Significant difference between depressed and non-depressed group on physical functioning ($U = 602$, $p < .05$), but not significant predictor of depression in regression model
				Depression & gender	Females more likely to be in depressed than non-depressed group ($\chi^2 = 5.89$, $p < .05$), but not significant predictor of depression in regression model

*Tseng, B.Y., Billinger, S.A., Gajewski, B.J., & Kluding, P.M. (2010). USA	Look at contributing factors to post-stroke exertion and chronic fatigue	n=21 Mean age = 59.5 years (sd10.3) Mean time since stroke = 4.1 (sd3.5 years)	Geriatric depression scale Fatigue severity scale	Fatigue & depression	Depression was significant predictor of fatigue ($\beta = .15$, $p < .01$)
*van de Port, I.G.L, Kwakkel, G., Bruin, M., & Linde The Netherlands	Look at factors associated with post-stroke depression	Prospective cohort study n=165 Mean age = 57 years	CES-D Fatigue severity scale Barthel index	Depression and fatigue Depression & physical functioning Depression & type of stroke	Fatigue was significant predictor of depression ($\beta = 1.32$, $p < .05$) No significant relationship observed No significant relationship observed
*Vuletic, V., Lezaic, Z., & Morovic, S. (2011). Croatia	Assess fatigue 3 months post-stroke	Mean age = 61.8 years (sd14.2) N=35	Hospital anxiety and depression scale Fatigue severity scale Multidimensional fatigue inventory Barthel index	Fatigue & depression Fatigue & physical functioning	Depression was significant predictor of fatigue ($\beta = -7.22$, $p < .05$) Significant negative correlation between fatigue & physical functioning ($p < .05$)
*Weaver, L.L., Page, S.J., Sheffler, L., & Chae, J. (2013). USA	Look at association between post-stroke depression, upper-extremity (UE) impairment, and UE motor function	n=118 Mean age not provided Mean time since stroke = 91.8 days	BDI-II Upper extremity section of the Fugl-Meyer assessment	Depression & lesion location Depression & gender	No significant relationship observed Females more depressed than males ($p < .01$)

*Winward, C., Sackley, C., Metha, Z., & Rothwell, P.M. (2009). UK	Look at factors associated with post-stroke fatigue by comparing those with minor stroke to those with TIA	n=76 Mean age = 74.2 years Assessed 6 months post-stroke	Chalder fatigue scale NIHSS	Fatigue & stroke severity	Prevalence of fatigue increased with stroke severity (OR = 6.96, 95%CI [1.3, 49.25], p < .01)
*Withall, A., Brodaty, H., Altendorf, A., & Sachdev, P.S. (2011).	Look at the relationship between post-stroke apathy and depression, and to examine the association with dementia	n=106 Assessed 3-6 months and 15 months post-stroke	SCID-DSM-IV criteria Apathy evaluation scale	Depression & Apathy	Depression and apathy can occur independently (OR = 1.79, 95% CI [0.48, 6.66])
*Yang, S., Hua, P., Shang, X., Hu, R., Mo, X. & Pan, X. (2013). China	Look at risk factors for post-stroke apathy and depression	n=75 Mean age = 66.7 years (sd9.3) Assessed within 7 days of stroke Ischemic stroke	Hamilton depression rating scale Apathy evaluation scale NIHSS	Apathy & Depression	Significant difference between those with and without apathy on depression (p < .05), depression significant predictor of post-stroke apathy (OR = 1.13, 95% CI [1.00, 1.27], p < .05)
				Apathy & lesion location	Significant difference between those with and without apathy on frontal area (p < .05)
				Depression & lesion location	No significant relationship observed

				Apathy & age Apathy & stroke severity Apathy & gender	Significant difference between those with and without apathy on age, those with apathy significantly older ($p < .01$) No significant relationship observed No significant difference observed
*Zhang, T., Jing, X., Zhao, X., Wang, C., Liu, Z., Zhou, Y., . . . Wang, Y. (2012). China	Look at radiological correlates of post-stroke depression	n=163 Assessed 3 months post-stroke Ischemic stroke	WHO-CIDI Neuropsychiatric inventory	Depression & lesion location	More frequent infarcts in frontal region in those with depression compared to those without ($p < .05$)
*Zhang, W-N, Pan, Y-H, Wang, X-Y, Zhao, Y. (2013). China	Look at incidence of post-stroke depression and its relationship with stroke characteristics	Prospective study n=91 Mean age = 60 years (sd10.4) Assessed within 2 weeks and at 3 months post-stroke Ischemic stroke	Hamilton depression rating scale WHO-CIDI NIHSS Modified Rankin scale	Depression & lesion location Depression & physical functioning Depression & gender	No significant relationship observed Low physical functioning significant predictor of depression (OR = 12.11, 95% CI [1.169,125.59], $p < .05$) Females more depressed than males ($\chi^2 = .75$, $p < .05$)

Appendix C

REC Approval Letter

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Appendix D

Kent R&D Approval

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Appendix E

Participant Information Sheet

Study Title: **Mood and tiredness following a stroke**

My name is Cliodhna Carroll and I am a trainee clinical psychologist at Canterbury Christ Church University.

I would like to invite you to take part in a research study. Before you decide if you would like to take part it is important that you understand why the research is being done and what it would involve for you.

Talk to others about the study if you wish, before you decide if you would like to take part. You may also wish to discuss it with your GP or another trusted health professional.

What is the purpose of the study?
The purpose of this study is to look at how your motivation, emotions and tiredness are related after having a stroke.

Why have I been invited?
You have been sent this invitation to take part in the study through a stroke charity or NHS stroke service which you may be involved with or registered with.
You have been asked if you would like to take part as you have had a stroke in the past.

Do I have to take part?
It is up to you to decide to take part in the study. If you agree to take part, I will then ask you to sign a consent form and return this to me.
You are free to withdraw at any time, without giving a reason. This would not affect the standard of care you receive.

What will happen to me if I take part?
If you decide to take part in the study, you will receive a booklet by post with a number of questionnaires for you to complete. These are standardised questionnaires asking about motivation, emotions and fatigue. You will also be asked to complete a number of questions about your most recent stroke.

You can ask a relative or friend to help you to complete these questionnaires, but the answers should be your own. It should take between 30 – 60 minutes to complete the questionnaires. You will receive a stamped addressed envelope for you to return the questionnaire to me.

What are the possible disadvantages and risks of taking part
We do not expect that taking part in this research will cause you undue distress. This study does not involve any treatments and involves completing questions about your motivation, emotions and tiredness. Should we identify a problem in relation to your mental health, we will contact you and advise you to contact your GP.
If you feel distressed after taking part you can contact me or contact a 24 hour helpline such

as the Samaritans on 0845 7 90 90 90 or East Kent Mental Health Matters phoneline on **0800 107 0160**

What are the possible benefits of taking part?
Taking part in this study may help you to better understand your motivation, mood and tiredness. In addition to this, it may help in the future, by helping us to understand the effects of having a stroke on motivation, mood and tiredness and how these may be related.

What will happen if I do not want to carry on with the study?
If you decide to withdraw from the study, we will destroy any information that you have provided.

What if there is a problem?
If you have a concern about any aspect of this study, you should first ask to speak to me and I will do my best to answer your questions. I can be contacted on 01892-507673.

Complaints
If you remain unhappy and wish to complain formally, you can do this by contacting Professor Paul Camic, Research Director, Department of Applied Psychology, Canterbury Christ Church University at 01892-507773.

Will my taking part in this study be kept confidential?
All information which is collected about you during the course of the research will be kept strictly confidential.

Your consent form and response booklet will both have a study number on them so that I can identify what consent form goes with the response booklet. This code will only be kept by me and will be held securely on a password protected computer file. It may be necessary for other authorised persons such as other researchers and regulatory authorities to have access to the information you have provided, but they will not be given your name or other identifying information.

Your consent form and response booklet will be stored separately in locked filing cabinets. The response booklet will only have your study number on it and no other personal details.

Details from the response booklet will be transferred to computer files and will be stored securely on a password-protected CD for 10 years. Paper copies will be destroyed securely on completion of the study.

You will be asked if you would like to receive information about further research studies. If you agree you may be contacted to take part in future research studies.
If you choose not to consent to taking part in further research, your consent forms and contact details will be destroyed securely at the completion of the study.

What will happen to the results of the research study?
The results from this research will be published in my doctoral thesis and in an academic journal. Results will also be published in newsletters of local stroke charities or services, such as East Kent Stroke.
You will not be identified in any report or publication resulting from this study.

Who is organising and funding the research?
This research is funded by Canterbury Christ Church University.

Who has reviewed the study?
All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and given favourable opinion by Queens Square, London Research Ethics Committee.

Further information and contact details
If you would like to speak to me and find out more about the study or have questions about it answered, you can leave a message for me on a 24-hour voicemail phone line at 01892 507673. Please say that the message is for me Cliodhna Carroll and leave a contact number so that I can get back to you or contact me by email on cc424@canterbury.ac.uk.

Appendix F

Consent Form

Study Number: 13/LO/0048
Participant Identification Number for this study:

Title of Project: Mood and tiredness following a stroke

Name of Researcher: Cliodhna Carroll, Trainee Clinical Psychologist

Please initial in box

1. I confirm that I have read and understand the information sheet dated 7th March, 2013 (version 2) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	
2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected.	
3. I understand that data collected during the study may be looked at by the research team. I give permission for the team to have access to my data.	
4. I agree to take part in the above study.	
5. I agree to receive information from one of the researchers about participating in future studies related to stroke.	
6. I acknowledge that data from this study will be published.	

Please turn over

Please print name	
Address	
Contact Phone Number	
Email address	

Please sign here:

Name of Participant	Date	Signature
Name of Person taking consent	Date	Signature

Appendix G
REC Substantial Amendment Favourable Opinion Letter

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Appendix H
Letter of Access

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Appendix I

Apathy Evaluation Scale (Self-rated)

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Appendix J

Geriatric Depression Scale

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Appendix K

Fatigue Severity Scale (FSS)

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Appendix L

Barthel Index

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Appendix M

Socio-Demographic Questionnaire

Title of Project: Mood and tiredness following a stroke

1. Age (In Years)		
2. Gender	**Male ( )**	**Female ( )**
3. Marital Status Please tick as appropriate	**Married ( )** **Civil Union ( )** **Co-Habiting ( )** **Divorced ( )** **Widowed ( )** **Single / Never Married ( )**	
4. Have you had more than one stroke? Please tick as appropriate	**No ( )**	**Yes ( )** **If yes, how many strokes have you had?** ____
6. How long is it since your last stroke? Please provide answer in years and months if possible	**____ Years ____ Months**	
Please answer the following questions in relation to your most recent stroke.		
7. Which side was your weakness on when you had your stroke?	**Left ( )**	**Right ( )**
8. BEFORE YOUR STROKE did you ever receive a diagnosis of a mental health problem?	**No ( )**	**Yes ( )**
8a. If you said yes to question 8, what was the diagnosis you received	**Anxiety** **Bipolar Disorder** **Depression**	**( )** **( )** **( )**

	Eating Disorder	( )
	Obsessive Compulsive Disorder	( )
	Personality Disorder	( )
	Phobia	( )
	Psychosis	( )
	Other	( ) **Please specify:**
9. At the time of your stroke what was your employment status?	**Employed**	( )
	Self-employed	( )
	Student	( )
	Unemployed – receiving state benefits	( )
	Unemployed – not receiving state benefits	( )
	Retired	( )
	Other	( ) **Please specify:**
9a. If you were retired at the time of your stroke, what was your employment status before you retired?	**Employed**	( )
	Self-employed	( )
	Student	( )
	Unemployed – receiving state benefits	( )
	Unemployed – not receiving state benefits	( )
	Other	( )

10. Please rate your general health at the time of your stroke	**( ) Excellent ( ) Good ( ) Fair ( ) Poor**	
11. BEFORE YOUR STROKE, did you have any of the following illnesses? *Please tick to indicate your response.*	**Acquired Brain Injury**	( )
	Anxiety	( )
	Depression	( )
	Dementia	( )
	Diabetes	( )
	Epilepsy	( )
	Fatigue	( )
	Heart disease	( )
	Hypertension	( )
	Myalgic Encephalopathy (ME)	( )
	Transient Ischemic Attack	( )
	Other health condition	( ) **Please specify:**
12. At the time of your stroke, where were you living?	**Alone in your own home**	( )
	Alone in rented property	( )
	With family in your own home	( )
	With family in rented property	( )
	Supported accommodation	( )
	Nursing home	( )
	Other	( ) **Please specify:**

13. What was your highest level of education achieved?	**Primary School** **Secondary School** **Third Level**	**( )** **( )** **( )**
14. Is English your first language?	**No ( )**	**Yes ( )**
14a. If you answered No to question 14, how long have you lived in the UK?	**____ Years**	

If you received help from a family member / carer with completing this questionnaire, please tick here ( )

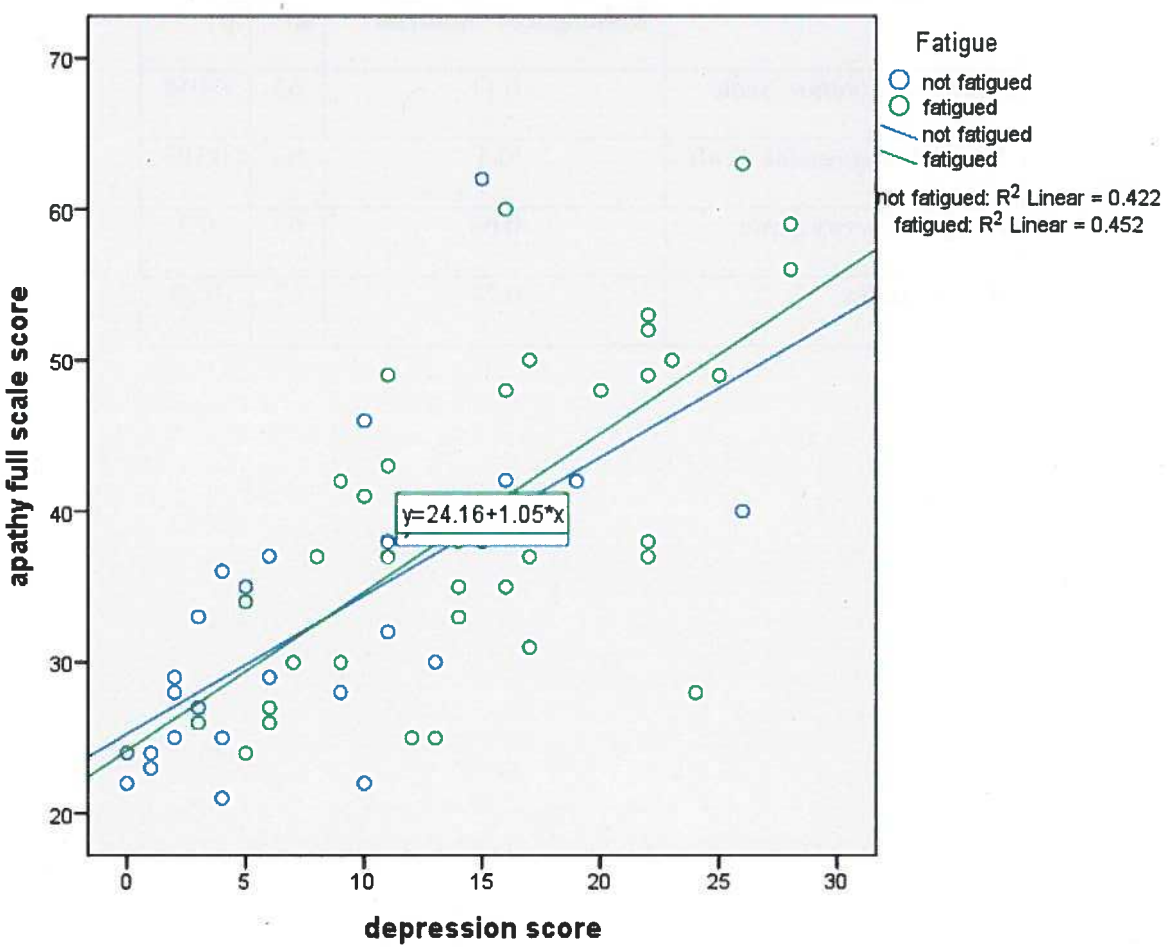
Appendix N

Tests of Normal Distribution

	Kolmogorov-Skmirnov	df	p
Apathy Evaluation Scale	0.11	63	0.059
Geriatric Depression Scale	0.1	63	0.193
Fatigue Severity Scale	0.08	63	0.2
Barthel Index	0.24	62	0.00

Appendix O

Scatterplot of Apathy and Depression accounting for Fatigue



Appendix P

Annual Progress Report to Main Research Ethics Committee

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Appendix Q

Report for R&D in Kent

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Appendix R

Summary Report to Recruiting Sites

Background: Stroke is a leading cause of disability in the UK and can lead to a number of physical, social and emotional difficulties. Problems with motivation, mood and tiredness are common consequences of stroke. Previous research has indicated that motivation and mood are related; and that mood and tiredness are related after stroke. However, to date no research has looked at how these three issues interact after stroke. This study aimed to address this gap in the research, and to examine what other factors might be linked to motivation, mood and tiredness after stroke.

What happened: Previous research in this area was reviewed, and a postal questionnaire was completed by 63 people aged over 55 years who had a stroke. This questionnaire involved completing commonly used assessment tools asking about motivation, mood and tiredness; and also some questions about the person's demographics and some details about their stroke.

Results: Previous research indicated that having poorer physical functioning, being female and have a more severe stroke were related to more problems with motivation, mood and tiredness after stroke. In the current study, 60.3% of people had problems with motivation, 58.6% had low mood and 58.7% had problems with tiredness. In this study, having poorer physical functioning was the only other factor which was associated with problems with motivation, low mood and tiredness. The relationships between low motivation, low mood, tiredness and poor physical functioning appeared to be somewhat different for men and women. For men, it seemed that having poorer physical functioning was more related to problems with tiredness than it was in women. This may have been due to men being more affected by the change in their roles and their mood being more affected by not being able to physically do the things which they could do prior to their stroke.

Conclusion: This research has implications in terms of how we understand the relationships between motivation, mood and tiredness after stroke. Health professionals working with people with stroke should consider these factors when developing interventions to help people who have had a stroke and are experiencing psychological difficulties.

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Appendix S

Author Guideline for Submission to 'Stroke'

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